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THE CLINICAL USE OF SULFANILAMIDE, SULFAPYRIDINE, SULFATHIAZOLE, SULFAGUANIDINE, AND SULFADIAZINE IN THE PROPHYLAXIS AND TREATMENT OF INFECTIONS*

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SHORTLY after the introduction of sulfanilamide it became evident, from the work of Marshall and his associates,[1, 2] that the rational use of this drug called for a knowledge of the factors concerning its absorption, distribution, excretion from the body, and the possible toxic effect which it might have. It quickly became evident that successful therapy with sulfanilamide depended upon the maintenance of certain concentrations of the drug in the blood of the patient under treatment. Later, with the introduction of sulfapyridine, sulfathiazole, sulfaguanidine,[3, 4] and sulfadiazine (2 sulfanilamidopyrimidine[5, 6]), and with the discovery that they presented different patterns in respect to their passage through the body from those of sulfanilamide, it has become necessary for the physician to possess a sound knowledge of the clinical pharmacology of these compounds if he expects to obtain the greatest measure of therapeutic success from their use. The problem as to which one of these compounds it is best to employ in a given infection is a real one. Hence, it is imperative when using these compounds to know of their behaviour in the body and to have the latest information regarding their comparative effectiveness in disease—types of data which can be based only upon extensive experimental investigations and sound clinical observations.

More is known about the fate of sulfanilamide in the human body than of any of the other compounds. This drug when administered by the oral route is well absorbed from the gastrointestinal tract, is fairly equally distributed throughout the body tissues, and if kidney function is normal is promptly excreted. The maintenance of adequate concentrations of sulfanilamide requires a dosage schedule that is on a four-hour basis. Sulfapyridine is irregularly absorbed by different individuals, and in the same individual the degree of absorption of this drug from the gastrointestinal tract may vary markedly from day to day. As far as information is available, the drug is fairly well distributed throughout the tissues, and as a general rule it is conjugated to the therapeutically inactive acetyl derivative in a much higher degree than is either sulfanilamide or sulfathiazole. From data available at the present time it seems that the liver plays the predominant rôle in the conjugation of sulfanilamide and its derivatives. Sulfapyridine is excreted more slowly than is sulfanilamide or sulfathiazole and in the urine a high percentage of the excreted drug is generally present in the acetylated form. This conjugated fraction is poorly soluble and tends to crystallize out in the urine.

Sulfathiazole is readily absorbed, and when kidney function is normal is rapidly excreted. It is conjugated by the tissues in about the same degree as has been noted for sulfanilamide. Data which have been obtained from the administration of the drug in patients whose kidney function is depressed and in whom the rate of excretion of the drug is decreased tend to show

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* This paper was presented before the Medico-Chirurgical Society of Ottawa, Canada, January 17, 1941.

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The experimental and clinical work upon sulfadiazine which is reported in this communication has been supported by a grant from the John and Mary R. Markle Foundation of New York City.

that if sulfathiazole remains in the body for any considerable period of time its rate of conjugation tends to increase rapidly. This suggests that the reason why sulfathiazole does not ordinarily seem to be converted in large amounts to the acetyl form is that the drug usually is excreted so rapidly that the conjugating mechanism in the liver does not have time to play its ordinary rôle. The drug is excreted almost entirely by the kidney, and in the urine definitely less sulfathiazole is found in the acetylated form than is the case with sulfapyridine, again, probably, because the drug is excreted so rapidly. This rapid excretion makes it difficult at times to maintain adequate concentrations of sulfathiazole in the blood. There is little information regarding the distribution of sulfathiazole in the tissues of the body. However, it is known that sulfathiazole passes over much less readily into the spinal fluid than does either sulfanilamide or sulfapyridine.

Sulfaguanidine introduces a new concept in bacterial chemotherapy, namely, that a drug given *per os* can be quite soluble in the stool, while at the same time its absorption from the gastrointestinal tract is limited. In patients total daily doses of sulfaguanidine up to 0.4 gram per kilo have been given with resulting concentrations of the drug in the blood of from 2 to 5 mg. per cent. Sulfaguanidine, apparently, is fairly well distributed through the tissues and is conjugated only to a moderate degree. That which is absorbed is excreted almost entirely in the urine, in which it exists as the free drug and the conjugated compound.

Sulfadiazine is fairly well absorbed by most patients, although its absorption is as a rule not as rapid as is that of sulfanilamide or sulfathiazole. In our experience, following the administration of single doses of the drug the peak concentration of sulfadiazine in the blood is reached between the sixth and eighth hours. Sulfadiazine is excreted mainly by the kidneys. Its rate of excretion is slower than that of sulfanilamide, sulfathiazole and sulfapyridine. Hence, it is easier to maintain adequate blood levels with this drug than it is with either sulfapyridine or sulfathiazole. Another factor of considerable importance is that acetylsulfadiazine is quite readily excreted by the kidney, and, therefore, unless kidney damage is present, very little of the conjugated drug is found in the blood. We have noted that even in the face of grave kidney damage the free and conjugated fractions of sulfadiazine seem to be more readily excreted by the damaged kidney than would have been expected were we dealing with sulfapyridine or sulfathiazole. At the present time, not enough information is available to permit one to say that less renal damage will occur in the course of sulfadiazine therapy, but if renal lesions due to drug toxicity are in part dependent upon the precipitation of the acetylated fractions of the drug, such as seems to be the case in the course of therapy with sulfapyridine or sulfathiazole, then sulfadiazine may cause less injury. This drug appears in the spinal fluid in about half the concentration that has been noted in blood taken at the same time. It apparently passes over fairly well into pleural exudates. It is excreted by the kidneys, and in the urine about two-thirds of sulfadiazine exists as the free form, while one-third is conjugated. At the present time data are not available for the clinical evaluation of this drug, but on the basis of the therapy of experimental infections one can say that sulfadiazine appears to be an effective chemotherapeutic agent in *E. coli,* hæmolytic streptococcal, pneumococcal, staphylococcal, *Cl. Welchii, Cl. septicum,* Friedländer's bacillary and colon bacillary infections in mice.

At the present time the sodium salts of sulfapyridine and sulfathiazole are available for therapeutic use. For parenteral administration, these compounds should be made up in 5 per cent solutions in distilled water, *and should always be administered by the intravenous route.* Immediately after these compounds pass into the blood stream, the sodium ion is split off, thus releasing either sulfapyridine or sulfathiazole as the case may be. From this point on these drugs behave in the tissues in a manner comparable to that noted when they are administered by the peroral route.

In the selection of the drug for the treatment of a given infection it is of the greatest importance that the correct etiological diagnosis of the disease process be made by bacteriological cultural methods. However, it is our firm opinion that one should never hesitate to employ these chemotherapeutic agents if he feels that, upon the basis of clinical diagnosis, an infection is present which is known to respond to sulfanilamide or its derivatives. The early use of these chemotherapeutic agents in the

TABLE I.

THE DRUG OF CHOICE IN THE PERORAL TREATMENT OF BACTERIAL INFECTIONS WHICH RESPOND WELL TO CHEMOTHERAPEUTIC AGENTS

Sulfanilamide	*Sulfapyridine*	*Sulfathiazole*	*Sulfaguanidine*
Chancroid	Gonococcal infections	*E. coli* tissue infection	Bacillary dysentery
Gas gangrene	Arthritis	Gonococcal infections	
Cl. Welchii	Endocarditis	Arthritis	
Hæmolytic streptococcal infections	Female gonorrhœa	Male gonorrhœa	
Abscesses	Male gonorrhœa	Pneumococcal infections	
Adenitis	Ophthalmia	Pneumonia	
Angina (Ludwig's)	Pneumococcal infections	Staphylococcal infections	
Cellulitis	Mastoiditis	Carbuncle	
Empyema	Meningitis	Cellulitis	
Erysipelas	Otitis media	Osteomyelitis	
Impetigo	Peritonitis	Pneumonia	
Lymphangitis	Pneumonia	Septicæmia	
Mastoiditis	Sinusitis (acute)	Urinary tract infections	
Meningitis	Staphylococcal infections	*A. ærogenes*	
Miscellaneous	Meningitis	*B. pyocyaneus*	
Osteomyelitis		*E. coli*	
Otitis media		*Staph. albus*	
Peritonitis		*Staph. aureus*	
Peritonsillar abscess			
Pharyngitis			
Pneumonia			
Puerperal sepsis			
Scarlet fever			
Septicæmia			
Sinusitis (acute)			
Tonsillitis			
Ulcers			
Lymphogranuloma Venereum			
Meningococcal infections			
Meningitis			
Septicæmia			
Streptococcus viridans infections			
Abscesses			
Cellulitis			
Meningitis			
Osteomyelitis			
Peridental infections			
Septicæmia			
Trachoma			
Urinary tract infections			
Hæmolytic streptococcal (Group B—)			
Proteus			

treatment of susceptible infections is of paramount importance if prompt, clear cut, clinical results are to be obtained. Recently, on the basis of experimental and clinical observations, we have attempted to list the drug of choice in the treatment of certain disease processes. We realize full well that there will be a definite disagreement on the part of some physicians concerning our evaluation of the clinical effectiveness of these drugs.

A question that frequently arises prior to the prescription of sulfanilamide or its derivatives to a given patient is, "Will an existing anæmia, leukopenia, hepatitis or nephritis be aggravated by therapy with these drugs?" The answer is "No" unless the patient is one of those unfortunates who is going to suffer from one or the other of the unpredictable toxic reactions of these drugs. We have repeatedly stressed this point because we feel that the only contraindication to the use of these drugs is that the patient has previously had one of them and has suffered from a toxic reaction to it. For this reason the physician must always ask a patient whether or not he has taken one of these drugs previously, and, if he has, whether he suffered a toxic reaction from it. If such a history is elicited it is best to give a small test dose of the drug (0.15 to 0.3 gram) and then observe the patient for acute toxic manifestations over a period of 12 hours before beginning the course of therapy. If none is observed

treatment may be cautiously begun and continued, a constant watch being kept for possible toxic manifestations.

In Table I are listed the drugs of choice in the peroral treatment of bacterial infections which are known to respond well to therapy with sulfanilamide or its derivatives. There can be little doubt, on the basis of present knowledge, that hæmolytic streptococcal infections produced by organisms belonging to Lancefield's Group A are best treated by sulfanilamide. The same seems to hold true for chancroid, Welch bacillus infections (gas gangrene), lymphogranuloma venereum, meningococcal infections, and infections (other than subacute bacterial endocarditis) which are produced by *S. viridans*, provided that the *S. viridans* belongs to the mouth group of these organisms and is not an enterococcus. At the present time it seems best that sulfanilamide be used in the therapy of trachoma and urinary tract infections due to the double zone-β hæmolytic streptococcus (Lancefield's Group B) or to *B. proteus*.

It is to be noted at this point that the use of sulfanilamide in the treatment of gonococcal infections is not recommended. This is based on the observations made by numerous workers during the past two years that sulfapyridine and sulfathiazole are definitely superior. Sulfapyridine, therefore, is an effective agent in the treatment of gonococcal infections, certain pneumococcal infections, and, because it passes readily into the spinal fluid, in staphylococcal meningitis.

There can be little doubt that sulfathiazole is the drug of choice in most staphylococcal infections. As for pneumococcal infections, it seems to be as effective in pneumococcal pneumonia as sulfapyridine, and it produces much less nausea and vomiting in patients. It seems to be as effective in male gonorrhœa as is sulfapyridine. From both the experimental and clinical points of view sulfathiazole appears to be the most effective drug in the treatment of colon bacillary infections of the tissues, such as peritonitis, pyelonephritis. In certain urinary tract infections it seems to be of considerable value.

Sulfaguanidine shows great promise of being an effective chemotherapeutic agent in the treatment of bacillary dysentery. At the present time the following dosage schedule seems to give good results. Initial dose, 0.1 gram per kilo of body weight, followed by 0.05 gram per kilo every 4 hours day and night until the stools are 4 or less per day; then 0.1 gram per kilo is given q. 8 hours day and night for at least 3 days, and, preferably, until the stools have become normal and the stool cultures are negative for dysentery bacilli.

TABLE II.

DISEASES IN WHICH THE PERORAL ADMINISTRATION OF SULFANILAMIDE OR ITS DERIVATIVES HAVE BEEN REPORTED TO BE OF SOME VALUE

Sulfanilamide	*Sulfapyridine*	*Sulfathiazole*
Actinomycosis	Brucella infections	Ulcerative colitis
Brucella infections	Dermatitis herpetiformis	
Hæmolytic streptococcal infections (Lancefield Groups B and C)	Friedländer's bacillus infections	
Influenza bacillus meningitis	Pemphigus	
Lupus erythematosis	Streptococcus viridans (Sub-acute bacterial endocarditis)	
Malaria	Ulcerative colitis	
Pemphigus		
Streptococcus viridans (Sub-acute bacterial endocarditis)		
Ulcerative colitis		

In Table II are listed certain diseases in which sulfanilamide or its derivatives have been used, but concerning which not enough reliable data are available to evaluate completely their clinical effects. Hence, one cannot recommend these drugs with the utmost confidence that they will accomplish the desired therapeutic results. It is our belief, however, that one should never hesitate at least to try the effects of these drugs in the diseases which have been listed here. The exception to this is malaria in which quinine,

TABLE III.

DISEASES IN WHICH SULFANILAMIDE OR ITS DERIVATIVES HAVE BEEN USED WITHOUT SATISFACTORILY DEMONSTRATING THEIR VALUE

Sulfanilamide	*Sulfapyridine*	*Sulfathiazole*
Anærobic streptococcal infections	Anærobic streptococcal infections	Anærobic streptococcal infections
Bacillary dysentery	Common colds	Influenza
Common colds	Influenza	Typhoid
Influenza	Paratyphoid fever	
Non-hæmolytic streptococcal infections	Chronic sinusitis	
Paratyphoid fever	Tularæmia	
Rheumatic fever (acute)	Typhoid	
Rocky Mountain spotted fever	Bacillary dysentery	
Chronic sinusitis		
Trichomonas vaginal infections		
Tuberculosis		
Tularæmia		
Typhoid		

atabrine, or plasmochin are always to be preferred.

In Table III are listed a number of diseases in which sulfanilamide or its derivatives have been tested, and in which there is no good evidence that they have a definite therapeutic value. For this reason their use in these diseases is not advised.

At this point it is important to remember that the rational and reasonable use of these drugs calls for more thought than just their correct prescription. One must not neglect the patient himself while treating a given infection, and all measures of proven value should be employed when indicated. Of considerable importance is the proper use of surgical procedures when such are advisable. This is especially true in the treatment of the complications of pneumonia, such as empyema, purulent arthritis, the drainage of abscesses occurring in the course of hæmolytic streptococcal infections, and especially the incision of purulent foci when sulfathiazole is being prescribed in staphylococcal infections. It has seemed to us that since the introduction of sulfathiazole possibly a little too much stress has been laid upon the chemotherapeutic activity of this drug in the therapy of staphylococcal infections. On several occasions we have seen individuals suffering from a staphylococcal bacteriæmia in whom the administration of the drug brought about a prompt clearing of the blood stream and signs of considerable improvement in the patient. However, in these patients the temperature and pulse did not come down to normal, and in hope that further administration of the drug would bring about the desired effect therapy was kept up over a period of weeks without complete recovery. Finally, sulfathiazole was stopped, and in each instance hidden and masked foci of infection began slowly to make their appearance. In all instances multiple surgical procedures were necessary before the patient recovered. These experiences lead us to believe that it is unwise to continue sulfathiazole over periods of weeks in staphylococcal infections unless there is definite clinical evidence that the patient is constantly improving.

The question of how much fluid should be given to patients who are receiving sulfanilamide or its derivatives is frequently of considerable importance. We have noted repeatedly patients in whom, despite apparently adequate doses of sulfanilamide, it seemed difficult to establish therapeutically active concentrations of sulfanilamide in the blood. In each instance it was found that the patients were receiving such large quantities (4,500 to 7,000 c.c.) of fluids each day that the drug was being excreted almost as rapidly as it was being absorbed. Hence, when patients are receiving sulfanilamide it is rarely necessary to force fluids beyond 3,500 c.c. per day.

When sulfapyridine or sulfathiazole is being given to a patient the administration of adequate amounts of fluids is a prime necessity. This results from the fact that in concentrated urines the precipitation of acetyl sulfapyridine or acetyl sulfathiazole is more likely to occur and, hence, there is a greater possibility of renal calculi being formed. Therefore, in patients who are receiving either of these drugs, *the urine output should be kept at 1,000 c.c. or more per day.*

Certain curious beliefs have grown up concerning the diets for patients who are receiving sulfanilamide or its derivatives. Eggs, for instance, are said to be dangerous because of their sulphur content, and because of the possibility that additions of sulphur will facilitate the production of sulphæmoglobin. It is sufficient to say that there are no data available to believe that such a superstition has any foundation in fact. It is probably a good thing to maintain an adequate vitamin intake in patients who are acutely or chronically ill with an infection and who are receiving one or the other of these drugs. We recommend that all such patients receive the following amount of vitamin each day during the course of their illness: vitamin A, 6,000 international units; thiamine chloride, 3 mg.; riboflavin, 3 mg.; nicotinic acid, 50 mg.; ascorbic acid, 100 mg.; vitamin D, 100 to 200 international units.

Also, so far as we know, there are no contraindications to the concurrent administration of other necessary drugs, provided that there are definite indications for such prescriptions. The possible exception to this statement is the use of *anæsthetic* (not sedative) doses of certain barbiturates in patients receiving sulfanilamide or its derivatives. However, one must bear in mind that it has been shown that patients who are receiving doses of sulfanilamide or sulfapyridine apparently suffer no ill effects from the administration of such anæsthetics as sodium pentothal.

Recently, considerable interest has been aroused in the local use of sulfanilamide and its derivatives in the treatment of superficial infections. At the present time our knowledge concerning the true value of these compounds when used locally is meagre. Jensen *et al.*[7] and Key and his associates[8] have shown that the local application of powdered sulfanilamide in cleanly debrided compound fractures markedly cuts down the incidence of infection in such types of wounds. Fragmentary reports from England are beginning to indicate that the local use of sulfanilamide and sulfapyridine in the prophylaxis of war wounds has resulted in a definite decrease in the incidence and severity of wound infection. In our own experience we have noted that streptococcal ulcers, indolent superficial staphylococcal infections, wounds and burns infected with mixtures of pathogenic micro-organisms often clear up promptly when treated locally with powdered sulfanilamide or its derivatives. While no definite information is available regarding optimal amounts of sulfanilamide or its derivatives for local use it has been suggested[9] that 0.10 gram per square inch of exposed tissue represents an adequate daily dose. On extensively debrided surfaces this can be sprayed on easily with a powder atomizer. It is probable that the main value of the local use of sulfanilamide or its derivatives is that it is possible to obtain relatively high concentrations of these drugs in the superficially infected tissues.

At the present time there is some controversy regarding the combined use of specific sera and antitoxins and sulfanilamide or its derivatives. In Table IV are given the indications for such combined uses. As may be seen from the table, only in patients severely ill with pneumococcal lobar pneumonia, or in patients moderately or severely ill with scarlet fever, is there definite information which leads us to believe that combined sero- and chemotherapy is of real value.

TABLE IV.

THE INDICATIONS FOR THE USE OF THERAPEUTIC ANTISERA WITH SULFANILAMIDE OR ITS DERIVATIVES

Gas gangrene—Adequate clinical data are not available.

Meningococcal infections—No conclusive clinical evidence that the combined meningococcal antiserum and sulfanilamide is better than sulfanilamide alone.

Pneumococcal lobar pneumonia—Patients who are severely ill should receive *adequate amounts* of type specific pneumococcal antiserum as well as full doses of sulfathiazole.

Staphylococcal infection—Clinical evidence as to the value of combined therapy is not available.

Scarlet fever—Patients who are moderately or severely ill should receive *adequate amounts* of scarlet fever antitoxin as well as sulfanilamide.

The indications for the prophylactic use of sulfanilamide or its derivatives have not been thoroughly established. In Table V we have listed the possible prophylactic uses of these drugs. It seems quite clear at the present time that the administration for a period of 10 days to 2 weeks of adequate doses of sulfanilamide (either perorally or locally) to patients suffering from compound fractures prevents the development of gas gangrene and probably other types of infection. There also seems to be good reason to believe that if the earliest stages of otitis media (that of the beginning earache) are treated with sulfanilamide or sulfathiazole for a period of 48 to 72 hours few children will develop purulent infections of the middle ear with the possible resulting train of complications. The observations of Ravdin and Lockwood show quite clearly that the routine use of adequate doses of sulfanilamide in the postoperative treatment of appendicitis has markedly decreased the morbidity and case fatality rate from peritonitis occurring as a complication of appendicitis. Also the work of Thomas *et al.*[10] and of Coburn and his associates[11] seems to point to the fact that in the northern half of this country the administration of small daily doses of sulfanilamide from October 1st to June 1st prevents the recurrence of the active manifestations of rheumatic fever in patients suffering from that disease. If these

TABLE V.

INDICATIONS FOR THE POSSIBLE PERORAL PROPHYLACTIC USE OF SULFANILAMIDE OR ITS DERIVATES

Sulfanilamide	*Sulfapyridine*	*Sulfathiazole*	*Sulfaguanidine*
Burns	Otitis Media	Burns	Large bowel resections
Compound fractures		Peritonitis (appendectomies, large bowel resections, etc.)	
Scarlet fever contacts when Dick test positive		Urinary tract infections (Urological operations)	
Extensive tissue injuries Accidental Operative			
Gunshot wounds			
Otitis media (earache)			
Peritonitis (appendectomies, large bowel resections, etc.)			
Rheumatic fever (quiescent stage)			

latter observations could be widely confirmed a most important prophylactic measure would be at our disposal.

The administration of sulfathiazole as a prophylactic agent to patients who are undergoing a resection of the large bowel, or who have the risk of developing peritonitis following operative procedures in the abdomen has seemed to be most effective in the Johns Hopkins Hospital during the past year. In those patients who have to undergo a resection of the large bowel the drug is started in doses of 1.0 gram every 4 hours on the afternoon prior to the day of operation, and is continued until about the sixth post-operative day. Sulfaguanidine has also been used successfully in the prophylaxis of infection following resection of the large bowel. When the drug is used in this manner,

TABLE VI.

THE DOSAGE OF SULFANILAMIDE

Sulfanilamide

A. Severe infections.
   Initial dose (oral): 0.10 gram per kilogram of body weight.
   Subsequent doses (oral): Total daily dose based on 0.10 gram per kilogram, this to be divided in 6 parts and given q. 4 h. day and night until 7 days of normal temperature have elapsed.

B. Mild and moderately severe infections.
   Total daily dose based on 0.10 gram per kilogram of body weight, this to be divided into 6 parts and given q. 4 h. day and night until 5 days of normal temperature have elapsed.

C. Hæmolytic streptococcal otitis media, mastoiditis or osteomyelitis present a special problem because these infections involve bone. Sulfanilamide should be continued in moderate doses for at least 10 days after a *clinical* cure has been effected.

TABLE VII.

THE DOSAGE OF SULFAPYRIDINE AND SULFATHIAZOLE

Pneumococcal pneumonia

A. Adults.
   Initial dose (oral) either 4.0 grams.
   Subsequent doses (oral) either drug. 1.0 gram q. 4 h. day and night until the temperature has been normal for 72 hours.

B. Infants and children.
   Initial dose (oral) either drug, 0.15 gram per kilogram up to 25 kilograms of body weight.
   Subsequent doses (oral) either drug. Total daily dose is based upon 0.15 gram per kilogram up to 25 kilograms of body weight, this to be divided into 4 parts and given q. 6 h. day and night until the temperature has been normal for 48 hours.

Staphylococcal pneumonia

A. Adults and children.
   Sulfathiazole is the drug of choice. If satisfactory response is not obtained increase the daily dose by 25 to 50 per cent. Continue until temperature has been normal for 5 days.

TABLE VIII.

THE DOSAGE OF SULFATHIAZOLE IN STAPHYLOCOCCAL INFECTIONS OTHER THAN PNEUMONIA

A. Chemotherapy should not be used for boils, mild furunculosis, etc.

B. *Adequate surgical therapy* should *always be used* in conjunction with chemotherapy.
   I. Diffuse staphylococcal cellulitis, lymphangitis, etc., in adults.
      Initial dose (oral): 4.0 grams.
      Subsequent doses: 1.5 grams q. 4 h. day and night until the infection has ceased spreading. Then 1.0 gram q. 4 h. day and night for 7 days.
   II. Staphylococcal bacteriæmia in adults.
      Initial dose (oral): 4.0 grams.
      Subsequent doses: 1.5 grams q. 4 h. until the temperature has been normal for 48 hours. Then 1.0 gram q. 4 h. for 14 days. Then 0.5 gram q. 4 h. for another 14 days.
   III. Staphylococcal infections in infants and children. The initial subsequent doses are reduced from those advised for adults in proportion to the weight of the infant or child.

TABLE IX.

THE DOSAGE OF SULFAPYRIDINE OR SULFATHIAZOLE IN THE TREATMENT OF GONORRHŒA IN THE MALE

Either drug may be used.

First day dose: 3.0 grams, *i.e.*, 0.5 grams at 3 hour intervals six times a day.

Subsequent doses (2nd to 10th days): 2.0 grams per day.

If by the 5th day of treatment a marked improvement in symptoms and signs of the disease has not taken place, shift to the other drug and carry on as outlined above. If a shift in medication has been made and after 5 days marked improvement is not observed, *stop drug therapy* and begin *conservative local treatment.* In any event *do not continue treatment with these drugs beyond 15 days in patients suffering from gonorrhœa.*

TABLE X.

THE PARENTERAL USE OF SULFANILAMIDE OR ITS DERIVATIVES

Sulfanilamide—To be used only when oral medication is impossible.
   Initial dose: 0.10 gram per kilogram of body weight made up in a 1 per cent solution in sterile physiological saline or 1/6 molar sodium racemic lactate.
   Subsequent doses: 0.05 to 0.075 gram per kilogram of body weight in a 1 per cent solution, q. 6 to 8 h.

It is best to give solutions of sulfanilamide by the subcutaneous route. Oral administration of sulfanilamide should be started as soon as possible.

Sodium Sulfapyridine or *Sodium Sulfathiazole*—To be used only when oral medication is impossible or satisfactory concentrations of the drug cannot be obtained by oral administration.
   Initial dose: 0.06 gram per kilogram of body weight of the sodium salt made up in a 5 per cent solution of *sterile freshly distilled water. Do not try to sterilize by autoclaving or boiling.*
   Subsequent doses: 0.03 gram per kilogram of body weight of the sodium salt in a 5 per cent solution repeated at about 6 hour intervals.

Always give slowly (10-15 minutes) by the intravenous route. Oral administration of sulfapyridine or sulfathiazole should be started *as soon as possible.*

the dosage is 0.1 gram per kilo of body weight per os every 8 hours day and night for 6 days prior to operation. Then, as soon as possible after operation the same doses of the drug are started again by mouth and are continued for from 5 to 7 post-operative days. The prophylactic effect of the drug when used in this fashion results from its ability to decrease markedly the "coliform" flora of the bowel. *Sulfaguanidine does not sterilize fæcal material.*

In Tables VI to X are shown amounts of sulfanilamide or its derivatives which we believe represent therapeutically effective doses for severe infections due to the hæmolytic streptococcus, the meningococcus, the Welch bacillus, the pneumococcus, the staphylococcus and the gonococcus, and for mild or moderately severe tissue infections in which therapy with these drugs is indicated. When one is prescribing sulfanilamide for the treatment of a severe infection it is highly important to give a large initial dose in order that a therapeutically efficient concentration of the drug may be obtained rapidly; then sufficient doses of the drug should be given at 4 hour intervals in order to maintain and augment the effect obtained by the initial dose. In general, in severe infections in which sulfanilamide is being employed as the drug of choice, a concentration of the drug of 10 mg. per cent in the blood should be maintained until a marked clinical improvement in the condition of the patient has been noted. Then the amount of the drug given each day may be slowly decreased. In milder tissue infections in which sulfanilamide is the drug of choice concentrations of around 5 mg. per cent of the drug should be maintained in the blood.

On the basis of our present knowledge it seems as though sulfapyridine and sulfathiazole were equally effective in the treatment of pneumococcal pneumonia, with sulfathiazole generally being the drug of choice because it is less likely to provoke nausea and vomiting. During the febrile period of the pneumonia the concentration of these drugs should be kept at 4 to 6 mg. per cent in the blood of the patient.

In staphylococcal infections, with the possible exception of staphylococcal meningitis, sulfathiazole should always be employed. The exception of staphylococcal meningitis is the result of the observation that *sulfathiazole does not pass over readily into the spinal fluid.* This drug should not be used in the treatment of small boils, mild furuncles, etc., which result from superficial infections with staphylococci, because the risk of toxic manifestations from sulfathiazole is greater than the therapeutic results which may be obtained. *It is also of extreme importance to remember that adequate surgical therapy should always be used in conjunction with chemotherapy in the treatment of staphylococcal infections,* and that when an apparent marked improvement has taken place in a patient severely ill with a staphylococcal infection, if the drug is discontinued too early, a recurrence of the infection is very likely to happen. On the basis of present data concentrations of 5 to 10 mg. per cent should be maintained in the blood of patients who are severely ill with staphylococcal infections. As has been pointed out, relatively low concentrations of the drug, 2 to 5 mg. per cent, are found in the blood of patients who are receiving sulfaguanidine. In patients ill with pneumonia and who are receiving sulfadiazine the blood levels should be maintained at from 7 to 10 mg. per cent. This can be quite easily accomplished in most adult patients by giving an initial dose of the drug of 4.0 grams followed by maintenance doses of 1.0 gram every 4 hours for the first 24 hours and then doses of 1.0 gram every 6 hours for as long as is necessary to complete the cure of the pneumococcal infection.

Sulfanilamide and the sodium salts of sulfapyridine and sulfathiazole may be given by the parenteral route. Sulfanilamide is best administered by the subcutaneous route, while sulfapyridine and sulfathiazole should always be given by the intravenous route. When these drugs are administered by these routes, it is always wise to begin the oral administration of the drug as soon as the patient's condition permits, because the peroral route of administration of these drugs is, in general, the most satisfactory.

In patients whose infections involve bone or bony tissue the use of these drugs presents a special problem because a recurrence of the infection is liable to take place unless all foci of infection have been eliminated. For this reason, again, adequate surgical drainage is important, and in such conditions as otitis media, mastoiditis or osteomyelitis, the administration of sulfanilamide or its derivatives should be continued in moderate doses for at

least 10 days after a *clinical cure has been effected.* The non-observance of this rule has been, in a large degree, the cause of the unsuccessful use of these drugs in otitis media or mastoiditis and for the reported masking of the symptoms and signs of these diseases.

One of the curious results of the intensive clinical work that has been done with sulfanilamide and its derivatives and of the publicity derived following such investigations during the past four years, has been to make physicians overcautious about the possible toxic manifestations of these drugs, while the patients, who read only of the "wonder drugs" in their local press, are clamoring for these agents whenever they have the mildest scratch in their throats or on their fingers. It is our opinion that we, as physicians, have been right in adopting a somewhat cautious attitude towards the use of these drugs, but we also feel that as our experience has grown it is now possible for the average physician to use these drugs intelligently even in the home, and that he should not worry too much about their possible toxic manifestations.

In Table XI are given the various manifestations of drug toxicity as we have noted them in hospitalized adults. It is evident from this table that the toxic reactions resulting from these drugs are quite frequent, but that those which are dangerous are relatively uncommon. It is our opinion that while it is

TABLE XI.

MANIFESTATIONS OF DRUG TOXICITY NOTED IN ADULTS TREATED WITH SULFANILAMIDE, SULFAPYRIDINE, SULFATHIAZOLE, SULFAGUANIDINE, OR SULFADIAZINE

Reaction	*Sulfanilamide*	*Sulfapyridine*	*Sulfathiazole*
Nausea, vomiting.	Fairly common.	Frequent.	Uncommon.
Dizziness.	Common.	Common.	Uncommon.
Psychoses.*	0.6 per cent; occur early.	0.3 per cent; occur early.	Rare.
Neuritis.**	Very rare.	Not reported.	Rare.
Cyanosis.	Very common, early and late.	Faint, common, early and late.	Uncommon.
Acidosis.*	1.9 per cent; occurs at any time; rare if soda is used.	Not reported.	Not reported.
Fever.*	10 per cent; generally 5th to 9th day; may occur 1st to 30th day.	4 per cent; generally 5th to 9th day; may occur 1st to 30th day.	10 per cent; generally 5th to 9th day.
Rash.*	1.9 per cent; may take any form, generally 5th to 9th day, may occur 1st to 30th day.	2 per cent; may take any form, 5th to 9th day, may occur 1st to 30th day.	5 per cent; nodular type common; may take any form, 5th to 9th day.
Hepatitis.**	0.6 per cent; early or late.	Not seen, but reported.	Rare.
Leukopenia with granulocytopenia.**	0.3 per cent; early or late.	0.6 per cent; early or late.	1.6 per cent; early or late.
Acute agranulocytosis.**	0.1 per cent; occurs 14th to 40th day, common 17th to 25th day.	0.3 per cent; occurs 14th to 40th day, common 17th to 25th day.	Not reported.
Mild hæmolytic anæmia.	3 per cent; early and late.	Rare.	Not reported.
Acute hæmolytic anæmia.**	1.8 per cent; occurs 1st to 5th day.	0.6 per cent; occurs 1st to 5th day.	Very rare.
Hæmaturia.*	Not reported.	8 per cent; generally early.	2.5 per cent; generally early.
Anuria with azotæmia.**	Not reported.	0.3 per cent; generally 1st 10 days.	0.7 per cent; generally 1st 10 days.
Hyperleukocytosis.*	Generally in presence of acute hæmolytic anæmia.	Generally in presence of acute hæmolytic anæmia.	Not reported.
Injection of scleræ and conjunctivæ.**	Not reported.	Not reported.	4 per cent; may occur with rash and fever, 5th to 9th day.
Purpura hæmorrhagica.**	Not seen, but reported.	Not seen, but reported.	Not reported.
Ocular and auditory disturbances.**	Rare.	Rare.	Very rare.
Jaundice.**	With acute hæmolytic anæmia or hepatitis.	With acute hæmolytic anæmia or hepatitis.	With acute hæmolytic anæmia or hepatitis.
Painful joints.*	Reported.	Not reported.	Reported with rash, etc.
Stomatitis.*	Rare.	Not reported.	Not reported.
Gastrointestinal tract disturbances.*	Bleeding rare, diarrhœa uncommon.	Rare.	Very rare.

*Best to stop drug and force fluids.
**Imperative to stop drug and force fluids.
Sulfaguanidine has shown little toxicity to date. Drug rash and fever have been noted.
Sulfadiazine seems to be well tolerated. We have noted one drug rash and fever in 40 patients who have received this drug.

always advisable whenever possible to utilize every available means of laboratory control in following a patient receiving sulfanilamide or its derivatives, practically all of the toxic reactions associated with the administration of these drugs can be detected by the physician if he exercises careful clinical control over his patient.

Patients who are receiving sulfanilamide or its derivatives for the first time *should be seen at least once a day*, and at this time the attending physician should inquire as to how the patient feels, with special reference to the symptoms of headache, body-aching or malaise, because these symptoms are the precursors of many of the toxic reactions of sulfanilamide or its derivatives. In addition to the inquiries concerning the patient's symptoms, the physician should carefully examine the scleræ for the presence of jaundice, and the conjunctivæ for injection or paleness. The presence of jaundiced scleræ with pale conjunctivæ probably means that an acute hæmolytic anæmia is developing. If the conjunctivæ are not pale, then the jaundice probably results from liver damage. The occurrence of injected conjunctivæ and scleræ, together with smarting and burning of the eyes, occurs as a toxic manifestation only in the course of sulfathiazole therapy. As an added check to the conjunctival examination the oral mucous membrane should be looked at, and inquiry should be made as to whether or not the patient is developing a sore throat. If the patient has been treated with sulfanilamide or one of its derivatives for more than a week, and while under treatment develops a moderately severe sore throat, this may indicate the beginning of an agranulocytosis, because, if he is being treated adequately, it would be quite unlikely that he would be getting a hæmolytic streptococcal sore throat. The skin of the body should always be looked at carefully for the presence of rash, because frequently in the early stage of such a toxic manifestation, the patient or his attendants will miss the fine macular eruption in the skin. At this point we can stress the importance of keeping patients who are receiving sulfanilamide or its derivatives out of the direct rays of the sun and away from sources of ultraviolet light, because there is no doubt that a certain number of patients who develop a skin rash in the course of therapy do so because of a photosensitization. Any patient receiving these drugs should stay out of the sun until three days after he has stopped taking the drug, or until after the time when the drug has been completely excreted.

The temperature should always be taken in order to detect whether drug-fever is present, and if the patient says he has been having chills, and at the time that it is taken the temperature is normal, arrangements should be made to have it taken frequently during the next 24 hours in order to determine whether or not fever is present.

In as much as sulfanilamide does not directly damage the kidneys no special precautions have to be observed in respect to the urine of patients who are receiving sulfanilamide, but it is very important that the urine of patients who are receiving sulfapyridine or sulfathiazole be looked at when freshly voided, and that the total urine output be measured daily. This can be done easily by the patient's attendants or family, and a urine volume of at least 1,000 c.c. per day should be maintained. If the urine output starts to drop and the fluid intake has been properly maintained in patients who are receiving sulfapyridine or sulfathiazole it is very good evidence that the drugs are damaging the kidneys, either due to a direct toxic effect upon the kidney epithelium or as a result of mechanical blockage by aggregations of acetyl sulfathiazole or acetyl sulfapyridine crystals. However, *in the face of a normal urine output the presence of these crystals in the voided urine should never be considered an indication for stopping the drug.* The appearance of gross blood in the urine at any time in the course of therapy with these drugs constitutes a good reason for stopping therapy.

Thus, it can be seen that, with the possible exception of leukopenia or agranulocytosis, all of the toxic reactions resulting from the administration of these drugs can be discovered if the patient is kept under careful observation during his course of treatment, and for this reason it has proved highly practical for careful physicians to employ these drugs in patients who are being treated in their homes. If toxic manifestations appear these drugs should be discontinued and fluids should be forced vigorously in order to eliminate them from the system as rapidly as possible.

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RÉSUMÉ

Cet article est tellement important qu'un résumé de quelques lignes ne lui rend pas justice. Il ressort toutefois de la lecture de cette contribution qu'avant de prescrire les médicaments dérivés de la sulfanilamide il importe de bien connaître leur comportement dans l'organisme, leur mode d'excrétion, leur taux de concentration et leurs indications particulières dans une maladie donnée.

La grande contre-indication est une réaction toxique antérieure avec le même médicament; dans ces cas, il faut procéder avec une infinie prudence. Il faut faire boire les malades abondamment en cours de de traitement. Il faut leur administrer concomitamment les vitamines A, B et D. Il faut connaître et rechercher les taux de concentration les meilleurs et les maintenir dans le sang, surtout au début du traitement; cette précaution est formelle. On commence à connaître de mieux en mieux les effets prophylactiques de cette médication. Toutes les méthodes chirurgicales de traitement concomitant doivent toujours être mises en œuvre. En présence d'une guérison clinique on aura de meilleurs résultats en continuant la médication, à petites doses, pendant une dizaine de jours. J. SAUCIER

SOME ASPECTS OF AVIATION MEDICINE

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AVIATION medicine as we know it today is concerned with two major aspects; that of studying means by which the flying personnel may be rendered essentially normal while in the air, and methods of treatment of the peculiar conditions which may be suffered by these individuals. The scope and complexity of the problems involved may, perhaps, be best illustrated by considering some of the more obvious factors which are experienced by the flying personnel on any flight. On service flights, of course, some of these factors are greatly increased.

A bombing crew receive their instructions to take-off at a certain time, in a certain aircraft, to ascend to a certain altitude, fly to a certain objective, carry out certain operations, and return to their home airport. It sounds simple, but let us consider what a young pilot, observer and air gunner are subjected to on their two to ten hour flight. These members of the crew have their own specific duties to perform, and each must accept the responsibility which has been placed in his hands. Although they may be stationed in England, Africa, Bermuda, or Canada, in winter or in summer, these men must enter their aircraft clothed to protect them against the cold which becomes intense at the higher altitudes. They are equipped with helmets, earphones, microphones, oxygen masks, goggles, heavy flying clothing, gloves, parachute packs, etc., enough to burden any man, but all necessary for their ultimate efficiency.

The pilot is responsible for his aircraft. He has, in a medium-sized bomber, some 60 instruments and as many more sequences to check on his starting, taxiing, turn, and take-off, and all of these to watch continually while in flight. In a four motored aircraft his task is that much more complicated. The completion of the return flight may be just as hazardous as the mission, since blackout, fog, and damage to airports may add to the pilot's difficulty in making a successful landing.

The observer, who is also the navigator, must plot the course of the aircraft and navigate the aircraft to the target. At this time he acts as the bomb-aimer and the ultimate success or failure of the flight depends upon his ability to accurately strike the target. Again he becomes navigator on the return flight.

The gunner during the actual flight acts in the capacity of gunner and wireless operator. In this capacity it is his responsibility to keep in communication with the other aircraft in the flight, with the home airport, and to pass the information so obtained on to the navigator and pilot. During attack the wireless air gunner,

who is continually scanning the skies, plays his heroic rôle of protecting the bomber from destruction by enemy aircraft.

So much for their general duties while in flight. Let us now consider some of the factors which affect the personnel in flight. In ascent an individual is immediately subjected to the mechanical effects of a decreased atmospheric pressure, and as the altitude is increased to 18,000 feet and higher the effects become more and more pronounced. "The volume of a gas varies inversely with the pressure". This of course means that at 18,000 feet, where the atmospheric pressure is approximately 380 mm. Hg., or ½ an atmosphere, the volume of the gases in the body is twice the volume it was at sea level (760 mm. Hg.). At 30,000 feet the pressure has been reduced to approximately 1/3 of an atmosphere. Associated with such changes in the atmospheric pressure is the increase in abdominal distension, with discomfort and perhaps pain. This abdominal distension may be directly responsible for alterations in or actual interference with respiration and circulation, with a subsequent decrease in efficiency of the individual.

The mechanical effects of the decreased atmospheric pressures are important but are insignificant when compared with the effects of the decrease in oxygen tension in the air which accompanies such low pressures. As far as is known, Boyle, in 1659, first showed that when air was gradually withdrawn from a chamber a point was reached where the air in the chamber would not support the life of a mouse or a small bird. At nearly this same point the flame of a burning candle went out. Naturally he concluded that as a result of decreasing the pressure something was extracted from the air which was essential to the burning candle and also essential for life. More than 200 years later Paul Bert proved on human subjects that unconsciousness and death resulted from exposures to high altitudes and made it known that oxygen was essential for life at altitudes above about 20,000 feet.

During the last war the aircraft were, as a rule, incapable of ascending to altitudes incompatible with life but numerous are the stories indicating loss of decision, poor vision, hilarity and euphoria, lassitude, decrease in concentration and co-ordination, etc., as a result of flying at 14,000 to 18,000 feet without oxygen. However, the value of oxygen was appreciated, and in the United States Air Service Medical Publication of that time we find: "From a practical standpoint it is now definitely determined that oxygen must be supplied to those flying above 15,000 feet. We advise our men to fix their masks in position before leaving the ground. It is best for the pilot to adjust the mask and wear it from the time he starts until he comes back." The prescribed oxygen unit of that time was equipped with a microphone enclosed in an oral-nasal mask which was both well designed and adequate for the oxygen concentrations required. With the necessity of having service aircraft capable of ascending to increasingly high altitudes a corresponding increase in the efficiency of oxygen masks, valves, types of oxygen supply, etc., is demanded. This demand has been met, and unless accidents occur to the oxygen equipment through shell fire, or the remote possibility of freezing, the flying personnel need not experience the effects of oxygen lack.

There are other factors, though, which contribute to loss of efficiency of all air-crews. As was mentioned previously the temperature of the atmosphere decreases rapidly with increasing altitudes. At 20,000 feet it is –25° C., while at 33,000 feet the temperature reaches a fairly stable minimum of –55° C. Associated with such changes in temperature the crew have to contend not only with bodily cold, but with continued interference of vision through fogging and later frosting over of windshields, gun turrets, etc. Loss of visibility of course means loss of efficiency and makes the mission not only more hazardous and nerve-wracking but often times useless. Glare and haze in daylight flying contribute greatly to the fatigue of the flying personnel and during night flying the blinding effect of searchlights, the continual changes of accommodation for near and light to far and darkness produces additional strains on the eyes. Vibration transmitted through the structure of the aircraft to the bony framework of the body is fatiguing to all members of the crew, but especially to the observer-navigator who must do his calculations sitting beside a rigidly mounted desk upon which his paper, pencils, instruments, and hand continually vibrate. The effect upon the eyes is apparent. Noise is something which we all understand, and most of us can accustom ourselves to almost any degree within 100 decibels. However, the effect of aircraft noise,

which is mostly propellor noise, on a person in an enclosed space is extremely fatiguing. In a prolonged flight and in such an enclosed space as an aircraft cabin, ventilation, heating, humidity control, the elimination of engine fumes and carbon monoxide, the optical qualities of transparent plastic, etc., become problems which have to be studied and solved by the engineers in association with the medical personnel familiar with such conditions.

For tactical reasons the speed of aircraft has increased tremendously and it is only recently that practical limitations have been discovered as a result of wind-tunnel work. By such means it has been shown that a condition of "compressibility burble" develops when the speed of the air passing over the aerofoil approximates the speed of sound. This results in a tremendous increase in "drag", and unless a radical change is made in the aerofoil will limit speeds in excess of 600 miles per hour. Speed in itself has little if any physiological effect upon the aircrew, but when the speed is directed in a new direction extremely high gravitational accelerations may develop, which, in turn, may produce the symptoms of "black-out" or even unconsciousness. It has been definitely stated in the German literature that accelerations in excess of 5 G (5 times the normal acceleration of gravity) will cause "black-out" symptoms in almost all pilots and that pull-outs from manœuvres where such forces are developed become dangerous. They advocate the crouching position (in a dive bomber) which places the pilot's head close to his knees. Such a position decreases the gravitational distance from head to heart and restricts the pooling of the blood in the splanchnic region. In certain tactical movements the ability of the pilot and the aircraft to withstand high forces of acceleration is of great advantage, but it appears that with the desire for more accurate dive-bombing the speed of descent is tending to be purposely decreased. However, the aircrew are still subjected to the repeated, fatiguing effects of these forces.

We must not, under any circumstance, neglect the psychological effects of high altitude upon the individual. Some very experienced pilots have a real "altitude fear" and going to altitudes in excess of 10,000 or 12,000 feet is not only a physical but a real mental effort. The effects of such a state of mind are obvious. The members of any aircrew, but especially the observer and the gunner, are liable to become air-sick. Air-sickness is a vague clinical entity associated with well-marked objective symptoms, in many respects resembling sea-sickness. Such a condition resulting from rough weather, tail-whips, nauseating engine fumes, psychological factors, etc., is not only fatiguing in the extreme but may render the subject completely incapable of carrying out his duties, with disastrous results.

All members of the crew must at all times be vigilant and ready to meet the enemy, must be continuously on the watch for ground flares, aircraft signals, and always scanning the skies for approaching enemy aircraft. These strains are present regardless of whether the aircraft is flying at 5,000 feet or 30,000 feet. It is obvious then that these men must possess good vision, good eye-muscle balance, good co-ordination, good colour perception, good dark adaptability, good hearing, good vaso-motor control and, in general, superb physical and mental stability. The effects on an individual of flying infrequently at great speeds and at high altitudes may not even be apparent, but when these conditions, plus the physical and mental strains of service flying, are experienced day after day, and perhaps many times on the same day, serious interference with aircrew efficiency results. Thus fatigue, in all its ramifications, becomes one of the major clinical entities in aviation medicine. Fatigue, although a clinical entity in itself, becomes as a result of the above conditions, one of the major symptoms of the newer clinical entity, chronic altitude or "decompression" sickness.

In order to better understand altitude sickness let us once more go back to Boyle's work in 1660, for it was he who gave us the first description of "aero-embolism" when he observed that bubbles appeared in the blood vessels and in the eyes of animals which had been subjected to rapid reduction of atmospheric pressure. He postulated that the bubbles were derived from the air which the blood had previously absorbed at ground level pressures. Today we have offered comparatively little to the advancement of that knowledge. However, it is now known that just as divers and caisson workers experience the "bends" or "caisson disease" when they come from an increased atmospheric pressure to sea-level pressure too quickly so do flying personnel experience a similar type of collapse when rapid ascent is made to high alti-

tudes. It is stated that nitrogen bubbles form, as a result of the decreased atmospheric pressure, in the central nervous system, in blood, in bones, in peripheral nerves, and in joints. Such bubble-formation may be gross and give rise to pain in joints, along the segmental distribution of a peripheral nerve, or even produce unconsciousness from central effects. In milder cases or those resulting from repeated exposures at lower altitudes, only a progressively increasing lassitude, fatigue, irritability, and desire for sleep may indicate a sub-acute or chronic type of altitude sickness. In such a condition, of course, the personnel are certainly incapable of performing their duties efficiently, and in some instances they may be completely incapacitated.

Perhaps now it is more readily appreciated that the medical examination for the selection of aircrew (observers, gunners and pilots) must be carefully performed, the standards must be high and rigidly adhered to. Some of those standards are undoubtedly arbitrary, but they are continuously undergoing changes as research in selection substantiates new standards or condemns old standards. But it must be remembered that the medical standards are based upon experience, and only research and more experience should be allowed to change them. Individuals who have organic disease, known or unknown to them, constitute a hazard not only to themselves but to others who may eventually be placed in the same bomber crew. For instance, an applicant may have passed his medical examination, later to be shown by electrocardiography to have evidence of diminished coronary artery blood flow or a bundle-branch block. Again, by electroencephalography an otherwise healthy, normal individual may be shown to have atypical "brain-waves". These two persons may be perfectly capable of carrying out essential ground duties, but they may, under the stress and excitement of service flying, perhaps more readily experience a faint or a cardiac accident.

Thus it can be seen that the problems which confront the Air Force medical officers are in a great many instances peculiar to the flying personnel. Such problems fall naturally into four main categories—those associated with selection of personnel, with training, with maintenance, and with service. In other words, our responsibility is to maintain the physical and mental health of our personnel at the highest possible level so that they may be able to take their place in the air for as many hours as possible, on as many days as possible, and with the greatest possible efficiency.

THE SOURCE AND PREVENTION OF SEPTIC INFECTION OF WOUNDS*

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IN a previous paper (Hare[1]) the importance of hæmolytic streptococcal infection of war wounds was pointed out together with suggestions as to the source of these organisms and possible methods for the prevention of infection. From the recent work of Miles *et al.*[2] there is reason to believe that despite the early use of sulfanilamide and related compounds, infections due to streptococci and staphylococci are as common in this war as in the last.

This paper is a preliminary report on studies carried out during the past year with a view to possible prevention of these infections by other means than chemotherapy. For this purpose the surgical staffs of the Toronto General Hospital, the Western Hospital, St. Michael's Hospital and the Hospital for Sick Children allowed us access to the cases in the emergency departments and all the infected cases in their wards. For these facilities we are naturally deeply grateful as we are also to the nursing staffs of these hospitals for their very willing co-operation. We were also accorded permission to obtain material from all wounds in two large industrial plants, and we would record our thanks to Dr. J. McKellar of the John Inglis Company and Dr. S. Thomson of the Massey-Harris Company for these facilities.

The streptococci and staphylococci which cause clinical infections of wounds.

The streptococci which cause infection of wounds are almost without exception beta hæmo-

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† Working with a grant from the National Research Council of Canada.

lytic and members of group A in the Lancefield-Hare scheme. They are identical with those which cause other infections such as scarlet fever, tonsillitis, erysipelas and puerperal fever. We shall refer to these strains as *Str. pyogenes.*

The staphylococci responsible for infection of wounds are almost invariably *Staph. aureus* and the criterion adopted for their differentiation from other forms of staphylococci has been ability to form coagulase.[3] *Staph. aureus* from wounds differs in no known way from those found in other forms of staphylococcal infection.

TABLE I.

PRESENCE OF HAEMOLYTIC STREPTOCOCCI IN RECENTLY INFLICTED WOUNDS

	Patients whose wounds were re-examined				*Patients whose wounds were not re-examined*	
		Initial examination	*Repeat examination*			
Type of accident	*Number*	*Number with hæmolytic streptococci*	*Number with hæmolytic streptococci*	*Number with hæmolytic streptococci who were clinically infected*	*Number*	*Number with hæmolytic streptococci*
Industrial.....	38	1 Group H	4 Group A	2	91	0
Street.....	25	0	0	0	44	0
Miscellaneous.....	17	0	0	0	29	0
Totals.....	80	1	4	2	164	0

THE SOURCE AND MODES OF INFECTION WITH STR. PYOGENES

For reasons given elsewhere[1] the wound is probably not infected at the time of infliction, for the air, the projectile, the soil and the dust, the clothing or the skin of normal persons are not infected with these organisms to any significant degree. Since that paper was written we have obtained further data in support of this which has recently been published (Hare[4]). Here we may mention that of 50 specimens of soil and dust from the streets none were found to contain hæmolytic streptococci. Of 121 pairs of trousers whose exterior surface was examined, not one was found to be contaminated with *Str. pyogenes* although other varieties of hæmolytic streptococci were present. Of 248 pairs of hands examined, 15 were found to have hæmolytic streptococci but only one of these strains was *Str. pyogenes,* and of 96 legs, 7 had hæmolytic streptococci but no *Str. pyogenes.*

We thus have a great deal of evidence that projectiles or the substances through which they pass on their way into a wound are not likely to be contaminated with *Str. pyogenes.* Further proof of this has been recently forthcoming in an investigation we are now making. Swabs were taken from all wounds immediately on arrival in the emergency department of the four hospitals and two industrial plants named above before anything whatever was done to the wounds. The time interval between infliction of the wound and its bacteriological examination was never more than 2 hours and usually a matter of a few minutes. The bacteriological results so far as they concern hæmolytic streptococci are given in Table I. It will be seen that of the 244 wounds examined only one was found to have hæmolytic streptococci in it and this strain was subsequently found to be a member of group H, a group whose members are almost without exception not pathogenic for human beings. The wound in question did not become infected.

The time at which hæmolytic streptococci enter the wounds from one of the sources to be discussed below probably varies greatly, and certainly any wound must be looked upon as being capable of infection until it is actually healed. In our series of wounds referred to in Table I, as many as possible were re-examined some time later (as far as possible 48 hours after infliction) in order to determine how many had become infected in the meanwhile. Of the 80 wounds so examined, 4 were found to have hæmolytic streptococci (all *Str. pyogenes*) in them, 3 having acquired them within 48 hours, but in the third, they were absent on the 6th day but present and causing clinical infection on the 10th day. These findings are complementary to those of Miles *et al.*[2] who found that

in wounds examined 1 to 3 days after infliction, 8.7 per cent had hæmolytic streptococci in them, whereas they were present in 18.5 per cent of those swabbed 4 to 12 days after and 20 per cent after 13 to 40 days. Thus there is evidently a tendency for the number of wounds in which hæmolytic streptococci are present to increase as the time interval increases between wounding and sampling, a finding similar to that of Fleming and Porteous[5] in the last war.

Thus the only logical conclusion that can be drawn is that *Str. pyogenes* is not present in the majority of wounds at the time of infliction, but is of exogenous origin. As pointed out below, nasopharyngeal carriers of *Str. pyogenes* form an exception for they may have the organisms on the skin or clothing and in such a person the organisms may naturally enter the wound at the time of infliction. But this does not account for all infections of these wounds, firstly because many casualties are not carriers, secondly because the incidence of infection in war time is far above the usual carrier rate for *Str. pyogenes,* thirdly because many carriers do not have the organisms on the skin or clothing, and fourthly because of the gradual increase in the number of casualties whose wounds become infected with hæmolytic streptococci with the passage of time.

Reservoirs of Str. pyogenes pathogenic for man.

The reservoirs of *Str. pyogenes* have been discussed in full by Hare.[1] Only two sources are known (1) the nasopharynx of cases, convalescents and carriers, and (2) pyogenic infections in human beings.

Evidence that infection of wounds may be due to transfer of Str. pyogenes from one of the above sources to a wound.

Except for the work of Miles *et al*[2] on hospital infections there is as yet little positive evidence in the particular case of wound infections. There is however much in regard to other streptococcal infections. The work of Smith,[6] Paine[7] and Dora Colebrook[8] has demonstrated beyond doubt the transfer of organisms from an attendant at the time of delivery to the birth canal as the cause of puerperal infections. Meleney and Stevens[9] have similarly drawn attention to the danger of the carrier in operating theatres as a cause of infection of clean operation wounds. But in addition, the whole of recent work on the epidemiology of streptococcal infection by Glover and Griffith,[10] Cruickshank and Godber,[11] Bradley[12] and others has demonstrated the importance of the throat carrier or air borne infection from suppurating cases as the source of many varieties of hæmolytic streptococcal infection.

Methods by which transfer of organisms from a reservoir to uninfected wounds takes place.

1. *Transfer from the nasopharynx.*—It can be shown that persons with *Str. pyogenes* in the throat expel the organisms when speaking, coughing or sneezing but not when breathing quietly.[13] The organisms are expelled inside relatively heavy droplets of spray so that when the operator or dresser bends over a wound and speaks he fulfils the best possible conditions for expelling organisms into it. No less than 8 out of 12 carriers tested in this way were able to expel the organisms when talking downwards on to a blood agar plate. In the same way, a casualty who is himself a nasopharyngeal carrier, may infect his own wound.

But there is an indirect route which in our opinion is as important if not more so than direct expulsion. For Hare[4] has recently shown that the hands, the clothing and the pockets of a nasopharyngeal carrier may be heavily contaminated with pathogenic strains of hæmolytic streptococci, and may remain in this condition for some considerable period of time. Such an individual may therefore infect an open wound if he handles it with ungloved hands. It was also shown in the same paper that a carrier may infect the bed and the room in which he sleeps, or even, as probably occurred in one case, the hands of a room mate. Clearly therefore the routes by which a nasopharyngeal carrier in the vicinity of an open wound may transfer his organisms to that wound are many and it is probably a matter of chance which is followed in any particular instance.

The possibility that a casualty who is already a carrier may become infected from the organisms on his own person has already been referred to.

2. *Transfer from purulent secretions of other infections.*—This of course may occur by way of the hands of the dresser or surgeon, by the use of inadequately sterilized instruments and conceivably by the use of second-hand dressings. Such routes are self evident and need no further comment. Other routes are however possible. It has for instance been shown by Cruickshank[14] that burns infected with *Str. pyogenes* may cause heavy contamination of the air of the ward and White[15] demonstrated the same to be true

TABLE II.

THE PRESENCE OF STR. PYOGENES ON AND IN THE SURROUNDINGS OF PATIENTS WITH INFECTED WOUNDS

Patient	*Diagnosis and duration of infection. Type of Str. pyogenes*	*Location of lesion*	*Type of treatment*	*Str. pyogenes in nasopharynx*	*Str. pyogenes on person*	*Str. pyogenes on bed clothes*	*Str. pyogenes in air of ward*
FIT	Chronic ulcers 3 months. 1 cm. diam. Type 12	1 – lateral aspect foot. 2 – buttocks.	Dry dressing.	.....	.....	Lower sheet. Type 12	1 colony 18″ away, Type 12. 1 colony on floor under bed, Type 12
BRO	Post-operative pelvic abscess 2 days. Type 12	Abdomen.	Dry dressing.	.....	.....	Lower sheet, spread, pillow, gloves worn to change dressing. All Type 12	.....
GOU	Chronic ulcer 4 weeks. 2 cm. diam. Not typed	Lateral malleolus.	Sulfanilamide paste.	.....	.....	.....	Not done.
HUN	Cellulitis 2 days. Type 1	Hand and arm.	Dry heat (cradle).	.....	.....	Lower sheet. Type 1 Spread. Type 1	2 colonies within 2′. Bedside, Type 1 2′ away, Type 5
CAR	Infected burn. Burned 10 days ago. Infection 2 days. Type 1	Leg, knee to ankle.	Tannic acid. After infection boracic compresses.	.....	Hands. Type 1	Lower sheet, bedspread. All Type 1	2 colonies within 18″. Type 1
POW	Tenosynovitis. Opened 1 day before. Type 5	Middle finger.	Alternating hot hand baths and heat cradle.	Nose. Type 5	.....	Upper sheet. Type 5 Spread. Heterologous Type	Not done.
WOL	Otitis media 2 weeks. Type 17	Ear.	Irrigations q. 4 hours. Absorbent cotton plug.	Nose. Type 17	.....	Pillow. Type 17	3 colonies within 5′. Type 17
CUP	Suppurating joint 2 days. Type 1	Knee.	Boracic compresses and heat cradle.	Throat. Type 5	.....	Lower sheet.	1 colony.
CAR	Adenitis. Open 1 day. Type 26	Submaxillary glands.	Boracic compresses.	Throat. Type 26	Mouth-corners, back, hands. Type 26	Upper sheet, lower sheet, pillow, spread. All Type 26	10 colonies within radius of 10′. All Type 26
HAY	Infected laceration (accidental). Type 12	Forearm.	Hot baths and heat cradle.	Throat. Type 12	.....	.....	.....
SMI	Bursitis. Not typed	Elbow.	Boracic compresses and moist heat.	Throat.	.....	.....	1 colony.
MUR	Ulcer 2″ diam. 2 to 3 days. Type 5	Malleolus.	Dry heat.	Nose and throat. Type 5	Saliva, legs. Type 5	Upper sheet, lower sheet. Both Type 5	3 colonies within 10′. Bedside colony Type 5. Bedside colony and distant Type 17
ELL	Infected compound fracture. Type 12	Femur.	Dry dressing.	Nose and throat. Type 12	Hair, upper lip, lower lip, mouth-corners, chest, leg. All Type 12	Lower and upper sheets, spread, pillow, gloves worn to change dressing. All Type 12	30 colonies within 5′. Type 12 2 days later 4 col. 11′. Type 12

of puerperal infections. The presence of the organisms in the air of wards in which there are infected wounds has been demonstrated by Miles *et al.*[2]

These workers did not show exactly how the organisms reached the atmosphere and an attempt has been made to elucidate this in an investigation of 13 cases with *Str. pyogenes* suppurating wounds in civil hospitals in Toronto. Bacteriological examinations were made of the hair, skin of the face, trunk, hands and legs of the patient, and of the upper and lower sheets of the bed, the pillow and the bedspread. In addition, blood agar plates were exposed at various places in the ward for two hours. The technical details are postponed to a later publication. Here we wish only to discuss the actual results obtained. These are summarized in Table II. It will be seen that in addition to the organisms in the secretions from the wounds, 4 had strains of the same type on various parts of their skin surface, 10 had them on the bedclothes and 9 out of 11 were contaminating the air of the ward in which they were lying. Eight of the patients had the organisms in their own nasopharynx but there was no evidence that these patients polluted their surroundings more heavily than those without them in the nose or throat. It is also of interest that in two cases, the outside of the dressings which appeared to be quite dry and uncontaminated were infected. Thus these studies show clearly that even small wounds, if infected, may cause pollution of the bedding and the atmosphere of the ward.

The method by which this widespread contamination of the surroundings may be achieved has also been studied. We have found that if dressings from an infected wound be hung in a wind tunnel along which a breeze of very low velocity (40 to 50 feet per minute) was passing, so long as the dressing is wet, few or no hæmolytic streptococci can be detected in the stream of air. If however it be allowed to dry even only at the edges, and then be agitated or merely folded for 2 minutes, quite large numbers (100 or more) of organisms may be picked up on plates held 3 metres away. In view of this it is quite easy to imagine the contamination of the bed, surrounding objects and the skin of the patient by his movements, during the dressing of the wound or while his bed is being made. Miles *et al.*, have actually demonstrated an increase in the microbic content of the air during bedmaking although they do not mention whether the number of hæmolytic streptococci was proportionately increased.

In regard to the latter point, we have exposed blood agar plates in a ward while the bed of a case with a discharging mastoid was being made. In the first series of exposures, the nurse made the bed with a minimum of disturbance quietly rolling the blanket and sheets off and avoiding any shaking of them. In the second series the bed was made with all the usual violence beloved of an efficient and hurried nurse. In one experiment, the number of colonies on the plates was 23 times greater during the violent bedmaking than during the quiet.

Thus air borne cross infection in surgical wards is perfectly feasible and in many ways it is surprising that in civil life it should occur so seldom.

Other routes have been suggested such as: instruments which may be improperly sterilized between cases, shears used for removing plaster casts, insufficient care of the drums of sterilized dressings. Baths may become contaminated and so cause cross infections. Bed pans, urine bottles and hand baths may likewise be channels of infection.

The relative importance of the different sources and the routes by which the organisms may reach the wound.

It is highly probable that along the lines of communication, infection of wounds by *Str. pyogenes* expelled from the nasopharynx of the man himself, one or other of the attendants, or indirectly by way of their hands are by far the most important, for during such time casualties are not likely to have any contact with an actively suppurating infection. Once in hospital, the same sources may still be responsible but an added menace is suppurating wounds amongst their neighbours in the ward and from the work of Miles *et al.*, there is no doubt that this occurs frequently. We still have insufficient data at our disposal to give any idea as to the relative importance of the different sources or the different routes. From Table II it would certainly appear that the patient's own nasopharynx may play an important and hitherto unsuspected part as the source of *Str. pyogenes* for infection of some wounds.

THE SOURCE AND MODE OF INFECTION WITH STAPHYLOCOCCI

Space does not permit of a detailed description of the results obtained with staphylococci. Suffice it to say that so far as our results go, they tend to indicate that the majority of these infections are also exogenous in origin. For in the examination of recently inflicted wounds, no less than 68 per cent were found to have staphylococci in them, but of 67 strains submitted to detailed examination, only 13 were found to be *Staph. aureus* (coagulase positive). The re-

mainder may be looked upon as not pathogenic. On the other hand, four patients whose wounds were examined soon after infliction did become infected with staphylococci during the succeeding period, the strains isolated during that time being all of them *Staph. aureus* (coagulase positive). Only one of them had had a similar coagulase positive strain at the time of infliction. Of the remainder, no staphylococci of any kind were isolated at the time of infliction from two, and in the third, *Staph. albus* only.

It would therefore seem that as with the hæmolytic streptococci, the organisms in many staphylococcal infections of wounds are also derived from exogenous sources of which the nose of the patient himself or an attendant and suppurating wounds in the neighbourhood are the most probable. Measures taken to prevent the ingress of hæmolytic streptococci should therefore largely prevent staphylococcal infection as well.

SUGGESTED MEASURES FOR THE PREVENTION OF INFECTION OF WOUNDS

1. FROM THE NASOPHARYNX OF CARRIERS.—Both direct expulsion of the organisms and their transfer by indirect contamination of the hands must be considered.

(*a*) *Direct expulsion of Str. pyogenes and Staph. aureus.*—The obvious method is the intelligent wearing of an efficient mask by all who at any time may come into contact with the wound. This is probably more important for the prevention of staphylococcal infection than streptococcal, but in any event we would hasten to condemn the practice of not wearing it over the nose because it is from the nose that staphylococci are expelled. In forward areas, we realize the wearing of masks may be difficult if not impossible but there is evidence that these organisms are expelled much less often if the operator refrains from speaking, coughing or sneezing, for which reason speaking should be discouraged when in the vicinity of open wounds.

All nasopharyngeal infections amongst the personnel of base hospitals in particular, and of more forward placed units if possible should be reported at once, the sufferer isolated and not until *Str. pyogenes* has been shown to be absent should he be allowed on duty. If this is impossible we suggest that he should wear a mask and gloves the whole of the time he is in the ward and if possible, be given work which does not necessitate his contact with wounds.

(*b*) *Indirect transfer by hands, clothing, etc.*—It is most inadvisable that the bare hands should at any time come into contact with open tissue without suitable treatment. The ideal measure to employ is the wearing of clean sterilized gloves renewed for each case by any one who attends wounds from the front line to base hospital until the wound is completely healed. If this is impossible, several alternatives may be suggested. Unsterilized gloves may be donned, washed thoroughly with soap and water, and then in an antiseptic of adequate strength, allowing it time to act (see Colebrook and Maxted[16]). If the wearing of gloves is impossible, the hands should at least be well washed in common soap and water. This alone may suffice to cleanse them of hæmolytic streptococci although it is doubtful whether they will be free of *Staph. aureus* after such treatment. Further treatment with an antiseptic such as Dettol, phenol, perchloride of mercury, etc., should then be carried out. Whichever of these antiseptics be employed it is again essential that they be allowed time to act.

The handkerchiefs of nasopharyngeal carriers can be shown to be contaminated, for which reason the use of handkerchiefs as an emergency dressing should be forbidden.

(*c*) *Transfer from a nasopharyngeal carrier not in direct contact with the patient.*—It is possible that a patient in a neighbouring bed may suffer a nasopharyngeal infection due to *Str. pyogenes* and bring about sufficient pollution of the atmosphere to cause infection in an open wound in a nearby patient. It is therefore desirable that all such patients be examined bacteriologically and, if necessary, isolated in order to guard against this type of infection. We have encountered one case in which an infection of a wound may have been due to the organisms from a nasopharyngeal infection in a patient who preceded him on the operating table.

2. FROM OTHER SUPPURATING WOUNDS IN THE NEIGHBOURHOOD.—As already pointed out, the organisms may be present in the nasopharynx of the wounded man, on the bedclothes and on the skin of various parts of the body surface as well as on the dressings. The whole of the patient, his bedding and the air surrounding him must therefore be looked upon as potentially infective for other persons. For these

reasons it is debatable whether such a person should be permitted in the vicinity of clean wounds. It is therefore suggested that all hospitals dealing with casualties be divided into two wings, one for clean and the other for infected cases. Preferably there should be a third or intermediate wing in which the patient is first put in order to determine the organisms causing the infection so that he can be transferred to the ward in the infected wing which deals with his particular organism.

The transfer of any patient from the clean to the infected wing should occur immediately on the appearance of fever, pain in the wound, etc., and should not wait for a bacteriological diagnosis to be made, a proceeding which in any event would require at least 24 hours. If it is possible to provide a third wing he should be transferred to it first while the bacteriological diagnosis is being made. The return of a patient from the infected wing to the clean should as a rule not be entertained unless a complete bacteriological examination of both wound and nasopharynx has been made. It is also suggested that any patient in the clean wing who manifests any sign of an upper respiratory tract infection should be examined bacteriologically and if possible placed in the intermediate wing until the absence of *Str. pyogenes* from his upper respiratory tract has been bacteriologically proved.

The measure proposed need not occasion any untoward dislocation of hospital routine for there is no reason why the two wings should be equal in size or that the beds allocated to septic cases be permanently so allocated. As soon as such a ward can be emptied it can be thoroughly cleaned along with its bedding and cases from incoming convoys used to fill it. It is however essential that as far as possible medical officers and nurses be allocated to either the infected or the clean wing and forbidden to attend patients in the other. This is necessary because of the very considerable danger that they may become temporary carriers or have their hands or their clothes contaminated and in this way transfer the infection to clean cases.

If circumstances arise when the above scheme cannot be applied the following points should be observed in order to avoid cross infection in wards in which both clean and infected cases are being nursed. (1) Clean, uninfected wounds should invariably be dressed first, before those which are infected. (2) No part of the dressings of infected cases should ever be handled by the bare hands. Gloves or preferably forceps should invariably be used. These must be suitably dealt with immediately the dressing is over. The infected dressings should be very carefully folded and placed in a covered receptacle at once. (3) Great care must be taken to disturb the bedclothes as little as possible when making the bed. Shaking or unnecessary agitation should be absolutely forbidden. Blankets, sheets and bedspreads should be carefully rolled off and as carefully rolled on again. Dirty sheets should not be deposited on the floor but placed with as little shaking or disturbance as possible into some suitable receptacle. Great care must be taken to avoid shaking the pillow case when removing the old one and putting a new one in place. (4) The floor should only be swept after a moist or oily dressing has been applied to keep the dust down. The same applies to dusting. In any event these activities should never be carried out at the time they usually are, before or during the time that wounds are being dressed; preferably they should be done last thing at night in order to allow the disturbed material time to settle out.

Finally we would suggest that no one measure will suddenly prevent sepsis in any wounds. The whole technique of wound treatment from the moment the wound in inflicted until it is finally healed should be such as to minimize as far as possible the danger of ingress of potentially pathognic organisms. We have no doubt whatever that in many respects the apparently adequate technique of peace time is in reality quite inadequate so that in time of stress as during war it breaks down completely. This is due, we are convinced, to the generally held belief that the organisms are already in the wound by the time it reaches hospital and it is therefore necessarily and inevitably doomed to infection. If this idea be abandoned, for it has no foundation in fact, the actual technique to be employed becomes a matter of common sense. But it seems to us that the first and essential step is a change in heart with regard to wound sepsis. The rest should be simple.

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SULFATHIAZOLE THERAPY OF GONORRHŒA

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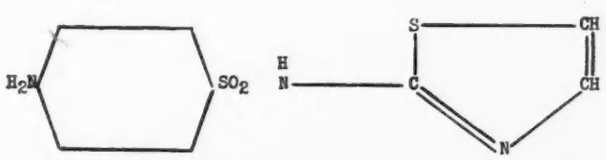
THE various sulfanilamide compounds used in the treatment of gonorrhœa have been highly effective in clearing up active symptoms of the disease. Not long after the discovery of the anti-bacterial properties of sulfanilamide, numerous related sulfanilamide compounds made their appearance. Each compound underwent exhaustive laboratory and clinical tests, and most were cast aside as not measuring up to the present day clinical standards.

Out of this vast array of compounds first came sulfapyridine, which is known all over the world for its therapeutic value in pneumococcal and gonococcal infections. The search for a chemotherapeutic agent of greater effectiveness and less toxicity than those now available continued. The most recent addition to this list is sulfathiazole, a sulfanilamide derivative, which appears to possess advantages over sulfapyridine.

Sulfathiazole is the thiazole analogue of sulfapyridine. It has the following structural formula.



Sulfathiazole was first described by Fosbinder and Water[5] in 1939. Long, Haviland, Edwards and Bliss[9] enumerated the clinical applications of sulfanilamide, sulfapyridine and sulfathiazole in March, 1940. They stated that sulfathiazole was effective against the streptococcus, pneumococcus, staphylococcus and colon bacillus infections.

The pharmacology of sulfathiazole has been carefully investigated by Van Dyke, Greep, Rake, and McKee[15] by Long, Haviland and Edwards[10] and by Barlow and Homburger.[2] These investigators often used sulfanilamide or sulfapyridine for comparison. Its chief advantages compared to sulfapyridine are believed to be: (1) more uniform absorption; (2) less conjugation after absorption so that a higher proportion of the total drug in the body-fluids is chemotherapeutically active; (3) less tendency to cause serious nausea or vomiting; and (4) greater effectiveness against the staphylococcus.

Pool and Cook,[13] in their paper on urinary tract infections, presented one case of gonorrhœa which was cured by the administration of sulfathiazole. Recent clinical reports indicate that sulfathiazole is particularly effective in the treatment of this disease. Excellent results have been presented by Stirling[14]; by Lloyd and Erskine[8]; by Mahoney, Wolcott and Van Slyke[11]; by Culp[4]; by Ballenger, McDonald and Coleman[1]; by Burkholder and Bang[3]; by Knight, Uhle and Latowsky[7]; and by Mitchell, Greig and Uren.[12]

The object of this report is to describe the experiences and results with sulfathiazole obtained in the treatment of gonorrhœa at the Toronto General Hospital. One hundred and twenty cases of gonorrhœal urethritis in the male are the basis for this report. In addition,

38 cases of non-specific urethritis cases in the male are presented.

The 120 male cases of gonorrhœa treated with sulfathiazole were obtained from routine admissions to the out-patient clinic. No selection of patients was made in this series. Cases of both acute and chronic gonorrhœa were included in the group. The duration of the urethral discharge varied from 1 day to 4 months, with 85 per cent confined to 7 days or less. The average age of the 120 cases was 25 years, but their ages varied from 14 to 65 years.

Of the 120 cases 96 had had no previous treatment with any chemotherapeutic agent. Twenty-four cases had previously failed to respond to one or more courses of sulfanilamide or sulfapyridine.

A positive diagnosis of gonorrhœa was obtained before sulfathiazole was started. A positive smear or culture of the urethral exudate was obtained in every case. Gonococci were demonstrated in the smears of those cases failing to have positive cultures.

Each patient in the early stages of treatment was seen at intervals of 2 days, and later at weekly intervals. On each return visit a careful urological examination was made, and urethral smears and cultures were obtained at appropriate intervals.

The patients were instructed to avoid alcohol, fatigue, heavy work, and abstain from sexual activity. The fluid intake was not limited.

The criteria of cure required that there be a complete absence of clinical evidence of the disease, that repeated smear and culture examinations be negative, and that the two-glass test of urine be free of pus and shreds. Patients were observed for a period of 6 weeks following cessation of chemotherapy.

Dosage.—The routine consisted of: 1st day—1 gram, 3 times a day after meals; 2nd and 3rd days—1 gram, 3 times a day after meals, and 1 gram on retiring; 4th and 5th days—1 gram, 3 times a day after meals.

It was decided to keep the dosage uniform, and not to administer the drug beyond the 5-day period if possible. The dosage can be prolonged, if so desired, although this is unnecessary in most instances. The reasons for not extending the drug beyond the 5-day period were: (1) it was apparent that if sulfathiazole was to be effective the patient was usually gonococcus-negative in an average of 3 days. (2) As we were dealing with ambulatory patients it was decided to give a dosage of the drug compatible with the normal activity of the patient. (3) Toxic reactions are rare before 5 days.

Of the 120 cases treated with sulfathiazole the majority received a total dosage of 17 grams in all. In some cases the amount administered varied considerably. In resistant cases the above course of treatment was either repeated or supplemented by the addition of 1.5 grams per day for an additional 7 to 10 days. The maximum amount given any patient was 51 grams.

RESULTS

The results of treatment of gonorrhœal urethritis in the male with sulfathiazole are summarized in Table I. Cures were obtained in 111 of 120 cases, indicating a gross cure rate of 92.5 per cent. Of this group of 120 cases, 24 had previously failed to respond to courses of sulfanilamide or sulfapyridine, and 22 (90.6 per cent) were cured with sulfathiazole. The remaining 96 cases had not been treated previously with any chemotherapeutic agent, and 89 (92.7 per cent) responded favourably.

TABLE I.

SUMMARY OF TREATMENT OF 120 CASES OF GONORRHŒAL URETHRITIS IN THE MALE TREATED WITH SULFATHIAZOLE.

Type of case	*Number of cases*	*Cured cases*		*Failures*	
		No.	*Percentage*	*No.*	*Percentage*
Total cases...	120	111	92.5	9	7.5
Previously untreated cases.	96	89	92.7	7	7.3
Previous sulfanilamide or sulfapyridine failures.....	24	22	90.6	2	9.4

Nine cases were failures. In 3 of these there was evidence that failure was due to re-infection, as they indulged in coitus during the early period of treatment. In 3 other cases the discharge recurred after an asymptomatic stage of the infection which lasted from 4 to 10 days after the drug was discontinued. Some of the failures were encountered in individuals who failed to co-operate in their treatment, or in those who indulged in excessive manual labour during the treatment.

In the cured cases the time-interval between the beginning of sulfathiazole therapy and the disappearance of discharge averaged 3 days and ranged from 1 to 7 days. No complications such as prostatitis or epididymitis developed in any of the cases during the period of treatment.

TOXIC MANIFESTATIONS

In 110 of the total number of 120 patients who were given a full course of sulfathiazole there were no symptoms of toxicity. In the remaining 10 patients, 3 complained of slight headache, 3 experienced vertigo, 2 suffered nausea, and 2 noticed slight drowsiness. The incidence of toxic reactions was 8.0 per cent. These symptoms were invariably mild, and did not in any way interfere with the normal daily activities of the patient.

Other toxic manifestations, sometimes mentioned, such as fever, rash, hæmaturia, injection of scleræ and conjunctivæ, anuria with azotæmia, leukopenia, granulocytopenia, and painful joints were not encountered in the present series.

NON-SPECIFIC URETHRITIS

The results of treatment of non-specific urethritis cases in the male with sulfathiazole are summarized in Table II. The dosage routine in these cases was the same as for the gonorrhœal cases, except that the above course was supplemented by the continued administration of 1.5 grams per day for a variable period of time. Of the 38 cases treated with sulfathiazole, the majority received a total dosage of 30 grams.

TABLE II.

SUMMARY OF TREATMENT OF 38 CASES OF NON-SPECIFIC URETHRITIS IN THE MALE TREATED WITH SULFATHIAZOLE.

Type of case	*Number of cases*		*Cured cases*		*Improved cases*		*Failures*	
	No.	*Per-centage*	*No.*	*Per-centage*	*No.*	*Per-centage*	*No.*	*Per-centage*
Non-specific urethritis.	38		21	55.3	9	23.7	8	21.0

Cures were obtained in 21 of 38 cases, indicating a gross cure rate of 55.3 per cent. Improvement was noticed in 9 cases, or 23.7 per cent. Eight cases (21.0 per cent) were failures.

In the cured cases the time-interval between the beginning of sulfathiazole therapy and the disappearance of discharge averaged 8 days.

TABLE III.

SUMMARY OF THE RESULTS OF TREATMENT OF GONORRHŒA BY CHEMOTHERAPEUTIC AGENTS AT THE TORONTO GENERAL HOSPITAL

Drug	*Total cases*	*Cured cases (percentage)*
Sulfanilamide.....	500	36 (77% improved)
Sulfapyridine.....	252	87
Sulfamethylthiazole.....	65	84
Sulfathiazole.....	120	92.5

SUMMARY AND CONCLUSIONS

1. The results in the treatment of 120 cases of gonorrhœal urethritis in the male treated with sulfathiazole are presented. The gross cure rate was 92.5 per cent. In the patients who had had no previous form of therapy the cure rate was 92.7 per cent. The group that had failed to respond to previous forms of chemotherapy did not show an appreciable fall in the cure rate.

The majority received an average of 17 grams of sulfathiazole and were cured within 3 days.

2. The use of sulfathiazole is associated with an unusual freedom from complications, so frequently encountered with gonorrhœa.

3. The occurrence of toxic reactions to sulfathiazole in the dosages recommended is slight.

4. Sulfathiazole appears to be a most efficient drug in the treatment of gonorrhœa. Its use is accompanied by a higher percentage of cures and a lower incidence of toxic effects than with any other chemotherapeutic agent.

5. A summary of the treatment of 38 cases of non-specific urethritis in the male treated with sulfathiazole is also presented. The cure rate in this group was lowered to 55.7 per cent, but an additional 23.7 per cent were greatly improved.

Sulfathiazole for preliminary investigation was kindly supplied by E. R. Squibb & Sons of Canada Ltd.

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SODIUM SULFATHIAZOLE IN UROLOGY*

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THE urethra is the initial proving ground for determining the potency of new compounds for chemotherapy in urology. If a new drug cures satisfactorily a higher percentage of patients than the previous best it becomes the basis for subsequent comparisons. This process had led to the gradual elimination of various compounds in the treatment of gonorrhœa, until at the present time the two most effective drugs are believed to be dagenan and sulfathiazole.

In our outdoor clinic sulfathiazole has proved slightly more effective than dagenan, and its use has been accompanied by fewer minor subjective symptoms. Patients able to avoid heavy exercise and to follow directions implicitly have been cured easily in about 90 per cent of the cases. There were 250 cases treated by dagenan, of which 87.5 per cent were cured, and 120 cases treated by sulfathiazole, with 92 per cent of cures. Some failures were due to lack of co-operation by the patient, sometimes unavoidable (riding a bicycle 24 miles a day, trucking, etc.), but for other failures there was no accounting. This 10 per cent gross failure by oral administration of the most effective drug not only presented a problem demanding more effective measures but provided an opportunity to study intravenous chemotherapy. The rationale for the use of parenteral therapy for such cases was based on the theory that failure of absorption of the drug or other miscarriage of therapy had occurred. All cases to be reported have been found resistant to orthodox treatment, except where stated.

The intravenous administration of a drug permits exact knowledge as to the amount of drug entering the blood stream, all of which amount is made available to excretion, and this almost entirely by the kidneys. There need be no question of failure as a result of poor absorption from the gastrointestinal tract. Many other considerations (passage through the stomach, etc.) are similarly eliminated, and it becomes simply a matter of giving the drug in sufficient quantity and for the required length of time to control and eradicate the infection. It is also just as true that infections not amenable to treatment by the sulfanilamide compounds can be recognized as such with more certainty. Earlier drugs did not lend themselves to this mode of administration because they were relatively insoluble; others were soluble enough, but toxic or ineffective.

Promin for intravenous use was supplied by Parke Davis, and its administration was begun, using fairly small dosage. The effects on gonorrhœa were prompt and consistent. However, recurrence of the gonorrhœa two or three days after apparent cure attended the use of this drug. In the hope of complete eradication of the gonococcus the amounts administered were increased, and treatment was prolonged well after the gonococcus had disappeared from the urethral smears. Some patients received as much as 1 gram per hour for 48 hours and were continued on smaller dosage for another 3 to 5 days. In spite of this intensive therapy, every patient showed recurrence of discharge and the organisms reappeared in 3 to 4 days. Some recurred while the drug administration was still being carried on. Promin intravenously was used effectively in some cases of acute pyelitis, but it was established

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conclusively that the drug was not suitable for the treatment of gonorrhœa.

This experience with promin prompted the investigation of soludagenan for gonorrhœal cases resistant to oral therapy. Once again treatment was begun with conservative dosage, three grams daily for one, two, or three consecutive days. This drug was found to be effective and adequate for cure in some cases. A good response was characterized by cessation of the discharge in 24 to 36 hours, and it was considered that cure was effected if there was no recurrence in 21 days. A small series of cases was observed on this drug with the following results, which were considered satisfactory and encouraging.

INTRAVENOUS DAGENAN

Gonorrhœa

Tl., aged 33. This patient received dagenan and prontylin in the Out-patient Department without effect. He was admitted to hospital and received 24 grams of promin on the 1st, 3rd, and 4th days, 72 grams in all. He appeared to have been cured as a result of this tremendous dosage, but had recurrence. Discharged, he responded immediately to sulfamethylthiazol in the Out-patient Department. This man received no soludagenan as we had not progressed to such therapy then (February, 1940). He was one of the last patients treated by promin. The large drug injection was actuated by the desire to give promin every possible chance to prove itself capable of curing gonorrhœa. After this failure, promin, although considered active, was regarded as lacking the potency to cure gonorrhœa.

Pi., aged 37. This patient was improved by oral sulfathiazole, but had some slight persistence of the disease with full recurrence when transferred to oral dagenan. He also developed prostatitis. Admitted to hospital all symptoms disappeared when 3 grams of soludagenan were administered on two successive days. There was recurrence, however, so Sitz baths, etc., were instituted. This was a case early in the use of soludagenan, and possibly had the intravenous therapy been continued cure might have been established thereby.

Bl., aged 35. This patient had discharge for 4 days, inguinal adenitis 2 days, and no therapy previous to admission. He was given 3 grams daily for 3 days. The discharge cleared in 48 hours. He was cured without further treatment.

Cr., aged 21. This patient had a discharge for 6 days not cured by sulfathiazole, dagenan, irrigation, instillations. He showed a good response to 3 grams of soludagenan daily, for 3 days, but the condition recurred. He was cured, however, by 6 grams of soludagenan daily for 3 days.

Pa., aged 43. Treatment with sulfathiazole and dagenan failed, and he was admitted. There was response to intravenous promin (48 grams), but the disease recurred. He was then cured by 18 grams of soludagenan, given 6 grams a day for 3 days.

These five cases illustrate the progression by clinical experience towards an adequate and safe dosage scheme of soludagenan for gonorrhœa.

Pyelonephritis—complicated

Wg. Pyelonephritis was present above a ureteral stone in an only kidney. Manipulation for stone was successful, but the pyelonephritis continued. Blood culture showed 42 colonies of *B. proteus* per c.c. Semicomatose, and the non-protein nitrogen rising (to 79), the patient was given 1 gram of soludagenan intravenously q. 4 h. x 6, with no benefit. He was given 1 gram, q. 4 h. x 6, of soludagenan intramuscularly. The patient died and no autopsy could be obtained. One, however, believed death was due to an acute suppurative pyelonephritis, the course of which was not influenced by the treatment.

Cellulitis

Or. This was a case of cellulitis of the scrotum and penis due to *S. hæmolyticus, Staph. aureus, B. coli,* a diphtheroid, and a Gram-negative fusiform bacillus. Multiple incision and drainage was carried out. Soludagenan, gram 1, was administered q. 3 h. x 12. He recovered. It was felt that the dagenan might have been the deciding factor of his recovery.

SODIUM SULFATHIAZOLE

Sulfathiazole, proving equally effective as dagenan in the oral treatment of gonorrhœa, was employed intravenously as the sodium salt, and a much larger series than with dagenan has been completed. Whether events will prove our impressions or not, it has also been our experience that this drug is less toxic than dagenan. This alone would give it preference, but we have clinical proof of its superior efficiency in the treatment of non-specific genito-urinary tract infections, and this, combined with its greater latitude of dosage, makes it the drug of choice.

The initial dosage was 3 grams daily on 3 successive days. This was fairly effective and well tolerated. The urethral discharge was slightly slower in disappearing (by 6 to 12 hours) than with dagenan. The dose was increased to 6, 3, 3 grams, and then to 6, 6, 6 grams on successive days, each increase producing earlier responses. This dosage was also well tolerated. The possibility of cure in 24 hours with the administration of 10 grams in 12 to 20 hours without further therapy occurred to us as feasible and was given trial.

The handling of the gonorrhœa patient is simple. He is given a bland diet and allowed fair mobility around his bed even while receiving treatment. Absolute recumbency allows some retention of exudate in the scrotal part of the urethra, and recumbency possibly is a factor in the development of renal crystallization of the drug. Certain it is that no severe reactions have been encountered as yet. The minor ones will be described.

Gonorrhœal urethritis

Twelve cases resistant to oral and local therapy were treated. They were all cured but three. One (J.L.) had not responded to dagenan, soludagenan, sulfathiazole by mouth, or routine local measures. He was given 20 grams of sulfathiazole intravenously, showed good response, but the condition recurred. A second course of 18 grams of sulfathiazole had no effect. He was finally cured by potassium permanganate irrigations. Why the patient failed to respond to the first series of irrigations and did to the second might be related to the effects of the first course of intravenous sulfathiazole. The second (R.J., aged 24), had failed to respond completely to oral sulfathiazole (two courses), probably because he persisted in riding a motorcycle. He had also received irrigations. Given soludagenan in hospital he was slightly improved. He was then given 10 grams of sulfathiazole in one day with no effect, so it was concluded that he was resistant to chemotherapy. He was finally cured by irrigations, which prior to the intravenous therapy had been ineffectual. The third (J.C.) had not responded to 17 grams of sulfathiazole administered in the Out-patient Department in the second week of the disease. Admitted to hospital, he was given repeated courses of intravenous therapy, to all of which there were good responses, but none to complete eradication of the gonococcus. These courses consisted of 10, 18, 18 grams of sodium sulfathiazole, 6 grams of soludagenan (sulfanilamide irrigations, no response), and 10, 48, 54 grams of sulfathiazole. This consumed several weeks of hospitalization. Irrigations of potassium permanganate and acriflavine instillations were not effective. Finally, under anæsthesia a No. 29 French sound was passed. The effect of this and 17 grams of sulfathiazole by mouth cured the patient.

The nine cases were of varying degrees of chronicity, some as long as one and half years associated with various complications, recent or remote. All responded promptly and completely to intravenous sodium sulfathiazole administered in various experimental dosage amounts. Four were given a single day of intensive therapy, 2 grams q. 2 h. 5, and of these three were cured without further treatment. The fourth had a second course of the usual three day administration of the drug, because although he showed a good response he had a recurrence of his disease three days after the one day of therapy. No further cures in 24 hours were attempted, because it seemed indicated to continue a small maintainance dose for 2 days to ensure complete eradication of the disease. One of the patients treated by the massive dose method had just finished a 5-day mapharsen course for primary lues. Thus his anti-luetic treatment and anti-gonococcal treatment were completed in 6½ days. His gonorrhœa was cured.

Two patients without previous oral or local therapy (transients admitted) were cured by 18 grams of sodium sulfathiazole. They were kept in hospital ten days after cessation of treatment. This interval seems more than enough, as all recurrences have been obvious two to three days after cessation of therapy.

These 14 cases of gonorrhœa have been treated by intravenous sodium sulfathiazole. Twelve were known to be resistant to all methods of treatment, except intravenous chemotherapy. Nine of the 12 were cured.

Non-specific urethritis

There were 5 cases of non-specific urethritis treated by sodium sulfathiazole at the same general dosage levels as above. They were given the treatment mainly in an effort to influence associated conditions.

Gn. Recurrent, non-specific periurethral abscess; pus already formed. There was no visible effect on the suppurative process, although the discharge was stopped.

Rt. This patient had non-specific urethritis persisting after specific infection; he also had gonococcal tenosynovitis. There had been no improvement in the tenosynovitis on dagenan, although it is reasonable to suppose it had cleared the gonococcus from the urethra, leaving the non-specific discharge persisting. This discharge was gone in 3 days after 18 grams of sodium sulfathiazole and did not recur. The tenosynovitis will be discussed later.

Cg. The associated condition was that of stricture. No response was elicited by oral medication. He had profuse discharge. Aged 61, he was given 4, 4, 4, 4 grams on successive days. The discharge ceased in 24 hours, but continued dosage was directed to the maximum improvement of the prostatitis. In this case the intravenous therapy was effective where the oral had failed.

Cy. and Ki. were acute (2 weeks) and chronic (3 months) urethridites. Both showed immediate and complete response with clearing of the discharge. Cy. going on to clear urine and Ki. to mucous shreds in the first glass. The predominating organism in urethral cultures was the *Staph. aureus* in both cases.

Epididymitis

1. *Acute specific.*—There were 6 cases. The clinical observation of these patients together with the subjective improvement suggested that

all benefited greatly from the intravenous administration of sodium sulfathiazole. All patients were free of the gonococcus in 24 to 36 hours. There were no recurrences. Pain in the scrotum was greatly diminished in 12 to 24 hours. In view of the progression of the disease to outlying structures each patient was given 3 and sometimes 4 days of treatment.

2. *Non-specific.*—One patient with very much swollen left-sided scrotal contents, fever 104 to 105° on admission, had normal temperature in 4 days and an almost normal epididymis in 8 days. It was felt that the drug had affected favourably the course of this particular case. In 5 other cases, however (none of which were so acute as the first), no beneficial effects were observed. One patient of the prostatitis cases, with old thickening of the epididymis (6 months) showed much less thickening of the epididymis two months after the drug therapy.

Prostatitis.—Two acute cases were treated. Both had dysuria, frequency, and fever. The infections were non-specific. Both showed immediate response to therapy, subjectively and clinically. Both voided more easily in less than 24 hours. The temperature came to normal in 2 and 3 days respectively, and they were discharged after a week in hospital. That their prostates were rendered free of pus is not known, and not likely, but certainly the course of the acute phase was greatly shortened.

Miscellaneous series

Post-operative cystitis.—One patient suffered from a chronic cystitis following operation upon the bladder. Multiple infecting organisms were present. He was given 6 grams intravenously in 2 days without appreciable effect. Therapy in this case was discontinued because of its toxic effect rather than for inefficiency. It was the last of a series of ineffectual methods of therapy in this particular case.

The second patient, aged 19, had a stubborn infection which showed no response to 13 grams. The etiology of this infection was obscure. Only a few *Staph. aurei* were to be found in the urine, but there were considerable amounts of pus. He was finally discharged unimproved.

Pyelonephritis.—Ss. Chronic infection of the kidney was aggravated by an unsuccessful manipulation for a large ureteral stone. Intravenous therapy had no influence on the duration of the fever. Other flare-ups were controlled as quickly and as easily by intravenous glucose alone. The predominating organism was *B. coli.* A second and similar case (Rg.), however, showed good response. The urine had *Staph. aureus.* Temperature, 104°, persisting 4 days on ordinary therapy, fell to normal, and the urine became sterile in 4 more days, with 22 grams of the drug. A third patient, moribund from suppurative bilateral pyelonephritis, showed no response to 6 grams rapidly given. He was dead in 24 hours.

Balanitis.—Gn. Acute suppurative gangrenous balanitis and proteolytic erosion of the glans showed no response whatsoever.

Soft chancre.—Ji. The patient had about twenty soft chancres. Specific organisms could not be found. His Wassermann test was 4 plus from a previous lesion. He had a keratinizing epithelioma of the glans. He received 10 grams of sodium sulfathiazole intravenously in 24 hours. Every ulcer responded immediately and appeared almost healed in 48 hours. They did not recur.

Arthritis.—Three cases were treated and all were benefited subjectively and objectively. The diagnosis in each case was that of gonorrhœal arthritis, but only one had the gonococcus in the urethral smears. There was a history of gonorrhœa in the other two, one recent (1 year) and one remote (7 years). There were, however, urethritis and prostatitis in all three.

Rn., aged 29, acute gonorrhœa with arthritis; no response to three courses of dagenan. He was given two courses of sulfathiazole, the first of which cured the discharge. He was admitted to hospital and received intravenously sodium sulfathiazole, with immediate response and complete cure of the arthritis in 7 days.

Ht. This patient, aged 35, had polyarthritis, with plantar fasciitis. The gonococcus was not isolated. He failed to respond to a month's oral chemotherapy and general measures. He was given 6, 4, 4, 4 grams of sodium sulfathiazole and showed immediate response. Now, at two months, there has been no recurrence of either the urethritis or the arthritis.

Jn. This case was similar to the previous one, (including the plantar fasciitis) except that he also had acute epididymitis and the joints involved were more acutely inflamed. He received 52 grams of sodium sulfathiazole. All the pain in the epididymis, right wrist, and heel subsided in 36 hours. He was up and about in the ward for one week without recurrence. He has not been seen since one month.

Tenosynovitis.—Rt. This patient, aged 36, had acute tenosynovitis of the long extensor and abductor of the thumb. All the pain was gone in 24 hours on sodium sulfathiazole, and full range of movement was restored in 4 days. Temperature of 100° came to normal in 24

hours. He had failed to respond to soludagenan. He received 3, 3, 3, 3 grams of sodium sulfathiazole in 4 days. There has been no recurrence in two months.

TOXIC REACTIONS FROM SODIUM SULFATHIAZOLE

1. *Chills.*—Two cases—Sd., and Ns., both probably were due to the glucose intravenous injection. As the drug was used from the bottom of the 200 gram frequently opened bottle the last few grams were sent for analysis. There had been no demonstrable chemical change (Squibbs).

2. *Rash.*—Jn. This one case developed a mild urticarial rash. He also had dagenan fever.

3. *Headaches.*—Gn., and Dr. In neither instance did they necessitate withdrawal of the drug.

There were no instances of cyanosis, anuria, hæmaturia, fever, neuritis, hæmolysis, jaundice, or agranulocytosis.

Injection of the drug has been accomplished by its solution in 1,500 or 2,000 c.c. of saline or 5 per cent glucose solution. It is felt that by the administration of this large amount of fluid and without restriction of fluid per os precipitation of the acetylated sulfathiazole has been avoided. Recently the intravenous administration has been reduced to 1,000 c.c. Still further reduction is under consideration in the hope that the continuous intravenous method may be discontinued in favour of individual injections by ampoule, as with soludagenan. With the rapid injection of 2 grams of sodium sulfathiazole higher blood concentrations of the drug will occur. If it is found that crystallization occurs with the concentrated drug injection more careful observation of the patient in this regard will be required.

RATE OF EXCRETION OF THE DRUG: BLOOD AND CEREBROSPINAL FLUID READINGS

Wr. This patient was given 6 grams in 1,000 c.c. glucose solution and blood and spinal fluid levels one-half hour after the drug was all in were 4.7 mg., and a trace only, respectively.

H.T. One patient, Ht., was given 6 grams intravenously in 1,000 c.c. glucose solution. Twelve hours after the therapy there was only 1 mg. per cent in the blood, and a trace in the spinal fluid.

Cn. This patient was given 10 grams in 1,000 c.c. of glucose solution. At twelve hours the blood and spinal fluid levels were 1.5 and 0.5 mg. per cent. All estimations were for free sulfathiazole.

SUMMARY

1. Intravenous therapy by promin gave promise of good affects to be obtained by this route of drug administration.

2. Soludagenan was adequate for cure in some cases of gonorrhœa resistant to oral therapy.

3. The effects of soludagenan on complicated pyelitis were not conclusive in the small series in which the drug was employed.

4. Sodium sulfathiazole cured 9 out of 12 patients resistant to all other methods of therapy. All three failures were affected in some way, however, that immediate cure was obtained by return to oral or local therapy, which had failed originally.

5. Two previously untreated cases of gonorrhœa were cured by 18 grams of sodium sulfathiazole, 6 grams administered daily for 3 days.

6. Some good effects were observed on non-specific urethritis, but associated suppurative conditions were not influenced.

7. Six cases of gonorrhœal epididymitis were cured, some by 3 and some by 4 days of treatment.

8. One case of acute non-specific epididymitis was greatly benefited by sodium sulfathiazole. Five cases of subacute epididymitis showed little or no response.

9. Two cases of acute prostatitis showed rapid and unusual improvement under sodium sulfathiazole.

10. Three cases of gonorrhœal arthritis were cured in 2, 3 and 7 days.

11. One of 3 cases of complicated pyelonephritis showed benefit from sodium sulfathiazole.

12. One case of gonorrhœal tenosynovitis was completely cured in 4 days, with maximum improvement in the first twenty-four hours.

13. Suppurative gangrenous balanitis was not influenced in one case.

14. Soft chancres, multiple, non-specific, were greatly benefited in the only case.

15. No beneficial effects were observed from the use of sodium sulfathiazole in two cases of cystitis, where the therapy was applied in the vain hope of beneficial effect which had been denied to various forms of orthodox treatment.

16. The toxic effects of sodium sulfathiazole were negligible. No crystallization of the sodium sulfathiazole severe enough to be recognized clinically occurred, probably because of the diuresis concomitant with the method of drug administration.

The Promin used in this work was kindly supplied by Parke Davis Co., the Soludagenan by Poulenc Frères and the Sulfathiazole by E. R. Squibb & Sons, to all of which firms we desire to express our thanks.

THE PHYSICIAN'S INTEREST IN GALL-BLADDER DISEASE*

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THE gall-bladder region of late years has been tacitly admitted to be within the sphere of influence if not in the actual possession of the surgeons. This does not however prevent the physician from having what might be called a benevolent interest in the region, and this interest arises from several sources. (1) He is interested in the problem of diagnosis, and the gall bladder enters as the unwanted child into a number of diagnostic problems. (2) He is interested in gall-bladder disease because it plays such a large part in his daily encounter with the matron who is fair, fat and forty, is belching gas, and cannot eat pork, pickles or pastry. (3) He is interested in disease of the gall bladder because of the diametrically opposed schools of procedure into which his surgical colleagues are divided upon the treatment of acute gall-bladder disease, and the proverb says that where certain people fall out, certain other people get what is coming to them, and so he—the physician—should be prepared to give a reasoned opinion in the individual case as between operative and non-operative treatment. (4) He is interested because of all the people who have proved gall-bladder disease some will not be subjected to operation, and may ask him what is to be done about it. (5) He is interested because of the view that gall-bladder disease has a harmful effect upon the myocardium, and that therefore in heart disease the abnormal gall bladder should be surgically removed.

Let us consider these subjects in a little more detail and first, the diagnosis of gall-bladder disease from other medical emergencies. Most medical men and some surgeons are like the Bourbons. They learn nothing and they forget nothing. Each of us has had some experiences, and some a whole gallery of experiences in which we have overlooked what was before our eyes, and all of us have failed to forget some of the preconceived ideas which time has proved to be fallacious, and it is this frailty of medical memory that justifies medical gatherings, where by the method of mutual reminder we may be helped to keep out of the rut of stratified error.

To return to the medical episodes which may be mistaken for acute gall-bladder disease. Perhaps the commonest is right lower lobe pneumonia. When pneumonia comes as the textbooks describe it, or when acute cholecystitis comes as the advance notices set it out, mistake is scarcely possible; but when each has shed its uniform, and frontal attack is discarded for guerilla warfare, and a pain appears over the upper right abdominal quadrant with fever and leucocytosis and slight jaundice, it's another story.

Even physicians have learned that blowing breathing and dullness are not the first signs of pneumonia, but, in their stead, limitation of movement on the affected side with suppressed breath sounds, with or without a few crepitations. And we have also learned that in pneumonia a slight icteroid tinge to the conjunctivæ is the rule rather than the exception, and that invariably, or as nearly invariably as is ever known in medicine, if there are referred pain and tenderness in the upper abdomen which originate in the chest, there will be also tenderness over the lower ribs in the axilla on that side.

Of all the signs however which assist in the diagnosis of gall-bladder disease from pneumonia the rapid respiration of the latter disease is the most useful. Much headway can be made in eliciting information from the history of an acute attack of pain in the upper abdomen by this simple group of questions: Did you groan? Did you writhe? Did you shiver? Did you vomit? Did you sweat? Did you faint? Did it hurt you to breathe?

Another decision which has to be made without undue delay, and in which if one is wrong he is very wrong, is the decision as to whether an acute cholecystitis or a coronary occlusion is the cause of an upper abdominal pain. Before 1912 we would have been afraid to make a diagnosis of coronary thrombosis, and in 1940 we are afraid not to make it, and it stands before us as a spectre when a patient complains of pain anywhere from the cricoid to the pubes. We

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will keep out of much trouble by asking the patient to place his hand over the site of pain and follow with the hand its radiation, rather than by asking him to state where the pain is; for topography and terminology have no meaning to the great majority of sick people.

The frontiers of coronary disease and cholecystic disease frequently overlap, but it is a rare event when the coronary victim does not first place his hand over the upper sternum, however much he may sweep it about from there outward or downward, and it is equally rare for the gall-bladder sufferer not to place his hand first over his epigastrium and sweep it then to right or left, and often behind and sometimes upward, but rarely farther up than the midsternum. But the rule does not work both ways. The coronary sufferer will often complain of his pain radiating down to the upper abdomen by which it may closely simulate acute gall-bladder disease. Th tenderness, the temperature, the leucocytosis, and the shock help to complete the illusion, as occurred in the following instance.

Some years ago a man of fifty-eight, who had had many attacks of cardiac pain, and had also suffered much from indigestion, had a spasm over the gall-bladder area with no substernal pain but with vomiting, fever, leucocytosis and profound collapse. The blood pressure was 165/130. The heart sounds were clear but distant and the pulse 120, and while we committed ourselves to a diagnosis of coronary disease, my surgical colleague and I felt certain that in addition he had an acutely inflamed, probably gangrenous gall bladder. His abdomen was opened and the gall bladder found tense but with no acute cholecystitis. He next morning developed a pericardial friction and died about twenty-four hours later with a most extensive cardiac infarction from coronary thrombosis.

Males over 50 are the probable subjects of coronary infarction, while women under 50 are the elected sufferers from gall-bladder disease, though every variety of exception may occur. The grey damp face, with its beseeching look, the almost complete immobility, the hand over the upper sternum, and in 20 per cent of cases the pericardial friction (only to be heard when searched for), all help in the distinction. The x-ray and the electrocardiogram are useful to the clinician but indispensable to all others.

Ernestene reports an instance of a solitary gall stone simulating coronary disease even to the extent of a pain radiating to both shoulders from the interscapular area, but there was no record of the pain being brought on by exertion. Removal of the stone removed the symptoms.

My scepticism as to the causing of the coronary syndrome by gall stones was increased by the case of a man with a typical anginal history and no evidence of cardiac disease, but x-ray evidence of a gall stone. This was removed and there was no recurrence of pain, but the man died suddenly a cardiac death 1½ years later.

The crises of tabes dorsalis have brought humiliation to the physician as much as pain to the patient, and their capacity to imitate the pains of gall-bladder disease is almost unlimited. They are not always lightning pains but may be severe and persistent, especially in the epigastrium, and associated with vomiting. Our protection against them is, first, the knowledge that they occur, and, second, our refusal to omit the routine examination of the patient in any instance of abdominal pain.

A surgical friend of mine at the end of his stay at a European clinic was presented by his preceptor with a reflex hammer and a flash light as a reminder of the two occasions on which he had mistaken tabetic crises for appendicitis. If this practice were general I would now have a good collection of these useful tools!

Lead poisoning comes into the same category as tabes as a cause of inexcusable error in the diagnosis of gall-bladder disease. The recalling of its possibility, and our examination of the gums are the two safeguards.

Diaphragmatic hernia may sometimes simulate gall-bladder disease.

A man of 57 who had had occasional glycosuria and occasional abdominal cramps was attacked suddenly by a severe wave-like pain working from the pubes to the ensiform. He became pale, perspiring and nauseated, but "could not vomit". He felt a "band" across his lumbar region. The pain lasted several hours and ceased suddenly. All laboratory and x-ray examinations showed no gall-bladder nor kidney disease, but x-ray of the stomach showed a diaphragmatic hernia.

Lately it has been pointed out that spontaneous pneumothorax on the right side may simulate biliary colic.

Stone in the right kidney or ureter, with or without infection of the urinary tract, will ordinarily offer little difficulty in the diagnosis from gall-bladder disease. The radiation of the pain, the local tenderness in the loin, and the things that one finds in the urine usually tell the story; but, just as renal infection may simulate pneumonia with great exactness, it may in some of its other irregularities simulate acute disease of the gall bladder, and in the absence of the x-ray, only a very careful review of the history and an equally painstaking bimanual palpation, with microscopical examination of the

urine, will give the answer. The distinction between gall-bladder disease and appendicitis, and between gall bladder disease and perforated peptic ulcer, are such frankly surgical matters that they will not be touched upon here.

Gall-bladder disease as a cause for the symptom-group known as "indigestion":—

For the most of us, from the standpoint of our day by day practice of medicine, the abdominal cavity and its contents might as well not exist if the pyloric and duodenal regions, the gall bladder and the appendix were left to us. By alkalinizing one and amputating the other two we would attempt to abolish 90 per cent of the abdominal ailments of which our patients complain. The 3½ pounds of liver, the ¼ pound of spleen, the 3 ounces of pancreas, and the 26 feet of intestinal tubing receive scant attention at our hands or from our heads, and if the hypothetical matron whom I mentioned before, still continues to belch gas after the duodenum, the gall bladder and the appendix have been taken care of, we are apt to call her a neurotic, give her luminal, and send her to the seaside.

Therefore, even if examination does show a poorly functioning gall bladder and it is removed, it is asking much that she shall have no more indigestion and no more gas. She and we will be most fortunate if that expected result occurs, and among the fortunate it does no doubt occur, but these are not the majority. We must remember that, except for the loss of her gall bladder, the woman is the same person she was before, with the same constitutional and metabolic faults, perhaps the same reasons that upset her gall bladder in the first place. The uncertainty of the outcome when cholecystectomy is done for this symptom of so-called indigestion should make us all chary in our promises of comfortable relief after operation.

The relief from attacks of gall-stone colic is another story, and if such attacks are frequent enough, definite enough, and crippling enough, they offer the best reason for surgical removal of the gall bladder for chronic disease.

This brings up the problem of what is to be done for the patient with acute cholecystitis.

A few years ago there wasn't any problem in this matter. One attempted and often succeeded in making a diagnosis between acute cholecystitis and acute appendicitis. If it was the former we advised non-surgical measures and left the gall bladder alone; if it was appendicitis we advised immediate operation. It seems but a short time ago that at a meeting like this my surgical colleague, an eminent and experienced member of the surgical fraternity, with emphasis and certainty expressed disapproval of surgical interference with an acutely inflamed gall bladder, going so far as to say that if he ever had inflammation of his gall bladder he would want a medical man and not a surgeon to look after him—perhaps an excusable heresy.

We are now faced with another point of view in surgical circles of which I speak only as a rank outsider. As typical of this view Heuer in 1937 pointed out that the clinical symptoms, the physical signs, and the laboratory data in acute cholecystitis often failed to indicate the course of the pathological process in the gall bladder, and that gangrene and perforation could occur even in the presence of subsiding and minimal symptoms. His statement that these complications occurred in 20 per cent of all cases of acute cholecystitis came as rather a surprise to me. From these facts and from the fact that the mortality of acute cholecystitis was 20 per cent in a large group of pooled cases, while in a group of 137 cases in which cholecystectomy had been performed before perforation had occurred the mortality was 2.1 per cent and in 16 cases which had perforated before operation the mortality was 12.5 per cent, he was encouraged to continue the practice of early operation in acute cholecystitis. Others take much the same ground as Heuer, but make the compromise that a period of 24 hours or more of observation is permissible to watch the clinical course of the disease and at the same time possibly to separate some cases in which operation may be safely delayed, and at the same time also, by the use of sugar and calcium, to improve the operative risk.

For one who has held for a life time to the idea that acute cholecystitis should be let alone until an abscess spouted under one's nose, it seems like backsliding to fall in with radicals who would remove the gall bladder as soon as a diagnosis of acute cholecystitis was made, but that is what has happened. There are some exceptions to this rule. One is the presence of other grave disease such as pneumonia or heart disease; another is the limited experience in abdominal surgery of the surgeon who is concerned. The gall bladder is one of several reasons why I am glad I am not a surgeon, and the removal of a distended and œdematous gall bladder from a

deep dark hole in a sick man, by one who is not very familiar with the road, is not a task for a schoolboy. For many years many people with acute cholecystitis have gotten well without operation, and unless the human and technical facilities are of the best the patient with acute cholecystitis is likely to be as safe under the conservative method as under the radical one.

I have purposely avoided in these remarks any detailed recital of statistics, neither will you hear anything about the laboratory methods in the diagnosis of gall-bladder disease, as I take it for granted that everyone is familiar with the routine of chemical and x-ray examination of the digestive tract.

Let us presume that by the help of all the methods at our disposal chronic cholecystitis has been diagnosed and for one reason or another operation is not advised or accepted. What is our procedure? As a rule the indications are very simple. People with chronic cholecystitis are usually, not always, inactive, greedy and obese. Inactivity may be due to coincident heart disease; if so, little can be done about it. If there is no heart weakness the patient should be persuaded, cajoled, or ordered to take regular moderate daily exercise on the level. Greediness is usually a biological trait, and the man who can make a greedy person eat less is wasting his time in medicine—he should be a ruler over 10 cities; but sometimes the miracle can be worked. Obesity is a natural consequence of the two faults of inactivity and overeating. The meals should be small and simple, free from complications, containing enough fat without being fatty, and, without the three "C's"—coffee, cocktails and condiments. Carbohydrates should predominate.

A small dose of a simple alkali, like the Sippy powder, may be taken between meals, and fluids should be taken freely. Most of the more complicated therapeutic methods are the accessories and paraphernalia of mental healing.

Between having gall-bladder disease and not having it there lies a kind of "no man's land" which has been called "dyskinesia", meaning defective emptying of the gall bladder and flaccidity as seen in the x-ray examination. In some instances there is an associated diminution of the gastric acidity, and in some the administration of olive oil before meals, combined with dilute hydrochloric acid has given symptomatic relief. Just what the actual significance of the so-called "dyskinesia" is remains an open question.

Certain signs suggest that operation should be considered. First: if pain replaces mild discomfort, or if colic is recurrent and disabling. Second: if loss of weight or strength is progressive.

Cancer of the gall bladder is relatively rare and is usually recognized too late, but careful observation of the weight curve and careful palpation of the gall bladder give us our surest clues.

Distension of the gall bladder is always an indication for operation. In the presence of known gall-bladder disease, fever and leucocytosis demand exploration, even in the absence of local tenderness, and as a rule a pericholecystic abscess will be found.

If operation is done for chronic disease and for the relief of discomfort the patient should be warned that while pain will likely disappear, flatulence may still remain.

Jaundice is a problem which concerns the physician, and it has close family ties with the gall bladder.

The question—"What are the varieties of jaundice?" has been the stock in trade of medical examiners since there were such things as medical examiners. About most of the varieties we are not going to worry now, but there are two in which the physician had better interest himself.

One is the slight and variable type of jaundice associated with a palpable, often firm liver, and stools which vary in their colour. Let us not lightly call these cases cirrhosis, and let it go at that. These may be types of so-called obstructive and infective jaundice, due to surgically relievable causes, and should not be ticketed as Hanot's or hypertrophic cirrhosis and permitted to drift, but after careful examination and reexamination the biliary tract should be explored.

One other variety is the persisting obstructive jaundice, and we recall Moynihan's statement that in such a case "No living man is infallible", and exploration should be our duty, sooner rather than later.

The newer knowledge of the dangers from bile salt lack in the bowel, and the fact that vitamin K, which helps to raise the prothrombin level and prevent hæmorrhage is inactive in the absence of bile, open our eyes to the dangers of prolonged biliary obstruction; and

even if the cause of the jaundice may not be removable, a surgical opening between bowel and gall bladder may not only relieve the symptoms of jaundice but prolong life.

There is put upon us also the duty of preparing people with jaundice for operation by the administration to them of the combination of bile and vitamin K, as well as of making sure that their reservoirs of salt and sugar and calcium are well filled.

The effect of gall bladder disease upon the heart.—

Much has been said on this subject, most of which is speculative and unproved. It is recognized that obesity is common to gall-bladder disease and to heart disease, and also that heart disease and gall-bladder disease appear most often after middle life, and for that reason they often appear together—so much so that the state of the heart should be carefully looked into in any candidate for gall-bladder operation. Acute cholecystitis will have the same unfavourable effect upon the circulatory system as any other febrile disease, but outside of this factor there is no valid reason for presuming that the gall bladder has any intimate association with myocardial efficiency, and so any surgical procedure on the gall bladder should be judged on its own merits, and not on any hypothetical benefit to the circulatory system. And what is said of the heart may be said of other efforts to assist nature by removing in the gall bladder a so-called focus of infection.

I never tire of quoting the saying of my teacher, James Stewart, that "The first aim of treatment is to prevent death", and the post-operative careers of people with the gall bladder removed do not always show that the heart is revitalized, that burping of gas has ceased, that old age is deferred, or that osteo-arthritis has disappeared. A disquieting number of people die of post-operative pulmonary diseases, or of the so-called "liver death", and others have stormy days of post-operative discomfort and the hearts of others do not stand the strain of rejuvenation.

Sometimes one seriously raises the question if "it were not better to bear the ills we have than to flee to others we know not of?" And in this instance a careful consideration of the *element of perspective* might preserve a number of middle-aged citizens to belch gas even to old age, rather than quell that belching prematurely and permanently.

RÉSUMÉ

Le médecin s'intéresse de plus en plus à la pathologie de la vésicule biliaire malgré que ce domaine appartienne virtuellement à la chirurgie, parce que les problèmes diagnostiques du carrefour hépato-biliaire englobent une grande partie de la pathologie abdominale. La plus fréquente méprise sera faite avec la pneumonie lobaire inférieure droite; dans ce cas, le meilleur élément de diagnostic de celle-ci est sûrement la tachypnée. Dans le cas d'occlusion coronarienne, le moyen le plus expéditif de résoudre la difficulté consistera à demander au malade d'indiquer avec sa main l'endroit où il souffre; dans les cas d'occlusion coronarienne il indiquera invariablement le sternum supérieur. Les calculs biliaires qui simulent les troubles coronariens demeurent l'exception. Les douleurs tabétiques seront aisément reconnues si l'on examine complètement le malade; il en va de même pour le saturnisme. La hernie diaphragmatique sera reconnue par la radiographie de l'estomac. Les calculs du rein et de l'uretère droits seront mis en lumière, surtout par un bon palper bi-manuel et l'analyse microscopique des urines. Plus difficile est l'appréciation exacte du syndrôme *indigestion;* diagnostic par élimination, avec ou sans résultats. Quant aux crises de colique hépatique, c'est leur répétition et leur gravité qui justifient l'intervention chirurgicale. Mais que doit-on faire devant une crise de cholécystite aigue? A la suite de Heuer, on a tendance à opérer tous ces malades, avec la réserve d'attendre 24 heures pour observer le cours des choses, et éventuellement éviter l'opération. La méthode conservatrice a encore beaucoup d'adeptes. Quant aux ictères, l'ictère léger et variable commande l'examen clinique minutieux des voies biliaires; l'ictère obstructif persistant nécessite l'exploration chirurgicale. Il faut préparer les sujets à opérer en leur donnant une combinaison de bile et de vitamine K; il faut, au surplus, s'enquérir parfaitement de la fonction cardiaque.

J. SAUCIER

Suggestions as to the more efficient prophylaxis of cerebrospinal fever have been made by the War Office as the result of experience gained during last winter's epidemic of the disease. Mass gargling and nasal insufflation on parade are no longer recommended, but open-air exercise is urged and the use of hot, humid, and stuffy rooms is deplored. Medical officers are advised to make sure that whenever rooms are vacated maximum ventilation is obtained, and during rush hours the occupants of the rooms should be dispersed as widely as possible and should avoid close contact around fires and in canteen bars. In the barrack rooms the centres of the beds should be six feet apart at least, and every alternate bed should be turned, so that each man sleeps with his head opposite his neighbour's feet.—*J. Roy. Inst. Pub. Health & Hygiene,* 1940, **3**: 295.

DIABETES MELLITUS: PROBLEMS OF ITS CONTROL*

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EIGHTEEN years ago last spring I saw the first child who ever had insulin. The late Professor McPhedran presented to his fifth year medical class of which I was a member a little diabetic boy who, in addition to the usual dietetic treatment had had two doses of "Banting's fluid". I should like to be able to say that we all realized that we were in the presence of a great discovery. On the contrary, with the usual barbarous ignorance of youth, we had our minds more on the time for the Saturday noon bell than on anything that our professor was telling us. It was not until later that we realized that the occasion had been historic.

This boy was 14 years old, had had diabetes for two years, and weighed 65 pounds on admission, his blood sugar was 580, on a diet of only 450 calories. He was admitted to hospital on December 2nd, and by January 11th it was evident that he was getting worse. He was given this pancreatic extract on January 11, 1922, the first dose being 15 c.c.

I come back to Toronto to talk about diabetes as a pilgrim comes to a shrine. As I go over to the old medical building where Banting did his first work on dogs do I find a tablet of any sort to mark the spot? No, we are too near the time. Events are not old enough to be historically venerated. In the Banting Institute there is a brick built into the wall from Lister's own ward in the Royal Infirmary in Glasgow. Future generations when building a medical school will ask for a brick from Banting's laboratory.

Our knowledge concerning diabetes mellitus has gone steadily forward since 1922. Because our knowledge has advanced we might reasonably hope that the diabetic death rate would fall. The very opposite is true. In common with that of other degenerative diseases the death rate from diabetes mellitus is increasing in Canada. In 1933 it was 12.1, in 1937 it was 14.

Now arises the question of the validity of vital statistics. Since, however, as Dublin once remarked, insulin does not confer immortality, the older patients sooner or later succumb to the degenerative diseases of their age, such as pneumonia, cancer, arteriosclerosis, and nephritis. Death certificates should clearly specify whether a death is from diabetes or with diabetes.

TABLE I.

DIABETIC DEATH RATE IN CANADA

1933	*1934*	*1935*	*1936*	*1937*
12.1	12.2	13.4	13.1	14.0

TABLE II.

DIABETIC DEATH RATE

	1934	*1938*
Nova Scotia	12.4	12.8
New Brunswick	11.5	13.7
Quebec (1935)	15.8	15.1
Ontario (1935)	14.5	15.6
Manitoba	9.7	10.4
Saskatchewan	8.9	8.0
Alberta	9.0	10.9
British Columbia	11.6	12.0

Diabetes in Canada receives preference in the tabulation of vital statistics over almost all local diseases. Diseases preferred to diabetes, when jointly stated, are cancer, tuberculosis, acute infectious diseases including influenza, lobar pneumonia; also coronary thrombosis, angina pectoris, tabes dorsalis, general paresis of the insane, acute intestinal obstruction, strangulated hernia, aneurysm, and puerperal sepsis.

In a study of diabetic deaths in Ontario in 1935 by Defries, Ross and Sellars, questioning of the physicians who signed the death certificates elicited the fact that the physicians really thought death was due to other causes than the diabetes in 245 of the 456 cases attributed by official practice to diabetes. In view of these facts the true diabetic death rate may not be so high as stated in official lists, but if these lists are not correct it is up to the doctors signing the death certificates to see that the certificates convey the true idea of the cause of death.

As we have said, the diabetic death rate is rising in Canada. Ontario has the highest rate and Saskatchewan the lowest. Since diabetes is a disease which appears for the most part between the ages of 50 and 60, and which causes

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death between 60 and 70 let us look at the relation between the diabetic death rate and the percentage of the population over 50 years of age and over 60 years.

TABLE III.

Province	*5 year average diabetic mortality rate*	*Percentage over 50 years*	*Percentage over 60 years*
Ontario	15.2	19.3	10.2
Nova Scotia	13.1	19.8	11.7
British Columbia	12.7	20.4	9.0
Quebec	12.2	14.0	7.2
New Brunswick	11.8	17.4	9.7
Manitoba	10.6	15.0	6.8
Alberta	9.4	13.6	5.7
Saskatchewan	8.9	15.5	6.5

The diabetic death rate follows fairly closely the proportion of those over 60 years.

The relation of the diabetic death rate to the cancer rate is interesting and follows it remarkably.

TABLE IV.

DEATH RATES

Province	*5 year average diabetes*	*1 year cancer*
Ontario	15.2	119
Nova Scotia	13.1	125
British Columbia	12.7	129
Quebec	12.2	100
New Brunswick	11.8	103
Manitoba	10.6	107
Alberta	9.4	87
Saskatchewan	8.9	68

Factors giving Saskatchewan a low diabetic death rate are (1) a young population, but this is not the whole answer, because Alberta has a younger population than Saskatchewan, and British Columbia, with the oldest population, does not have the highest diabetic death rate.

Joslin has a theory that luxurious living produces diabetes. He says "wherever and whenever conditions of life are easy, food abundant and relatively cheap over long periods, and when large numbers of individuals become accustomed to partake of food in excess of their requirements for the expenditure of energy, the frequent development of overweight and diabetes is favoured". This is an attractive theory and would seem to fit facts in Canada. Wealthy Ontario has a high diabetic death rate; poverty-stricken Saskatchewan has a low rate. But I do not believe this theory is true. Diabetes is not confined to the well-to-do. It is the rich woman who can afford to employ others to do her routine work, while she keeps her weight down on the Badminton courts and on the golf course. The rich can afford lettuce and tomatoes and fruit, while the poor must eat bread and porridge and potatoes and salt pork. Low calorie foods which are tasty and satisfying are expensive.

Joslin finds a higher incidence of diabetes in the wealthy eastern States than in the poorer mid-west, and concludes that high income is a factor in production of diabetes. I think the explanation is to be found in the fact that people are older in the east and again in the far west—California—than in the mid-west. Easy living is seldom a factor in development of diabetes in my cases. When a woman has raised sixteen children and has done all her own work on a prairie farm this could not be called easy living. Another factor helping our low diabetic death rate is the mental and moral quality of the population. Our people are either pioneers or the children of pioneers.

TABLE V.

BIRTH PLACE OF 153 DIABETIC PATIENTS WHOSE DISEASE APPEARED AFTER 50

Ontario	66	Belgium	2
England	22	Ireland	2
U.S.A.	13	Poland	2
Russia	9	Wales	1
Austria	8	China	1
Scotland	7	Hungary	1
Quebec	6	Serbia	1
Germany	6	New Brunswick	1
Nova Scotia	4	Sweden	1

Now there are two theories about pioneers. One is that if they had been any good they could have earned a living where they were born; the other is that they are adventurous and superior in type. Whatever theory you hold, you must admit that pioneers have that quality of hardness, that capacity for sticking to routine and for saying "no" which is essential to the successful diabetic. Diabetes is a disease in which the patient is not a passive being, as in the case, say, of an appendectomy. Diabetes requires co-operation on the part of the patient for 24 hours a day.

We see very few patients in Saskatchewan who are beyond the appreciation of the problem of what it means to stay on diet and to do tests. In large centres like Philadelphia, Boston and Toronto there is a hopeless, stupid, element, the dregs of society, which is not numerous in the west. Many of our people who are poor now were not so, ten, fifteen or twenty years ago. They have not the resigned outlook which goes with generations of poverty. A year's patients

seen in private practice give a fair cross-section of western diabetics. Of 44 new patients seen in 1939 two died, one of cancer, and one of staphylococcus septicæmia present when first seen. Two gave no co-operation; one of these felt that the condition was not serious, the other was of a poor type and was a religious cultist who refused insulin, saying that faith would heal him.

Four gave poor co-operation; one of these is a diabetic dwarf who also has nephritis; 1 is a man of 29 who has an ulcer of the stomach; 2 are middle-aged women, but they have interested relatives who will see they do not wander too far from treatment; one of these women is 70, with nephritis and hypertension. This gives 84 per cent of patients who are co-operative. Seven of this series are severe diabetics. My definition of a severe diabetic is one who is sugar-free on unmodified insulin at 10 p.m. and without ingesting any food shows sugar before breakfast.

Probably another factor in the low Saskatchewan death rate is the continuous propaganda. We constantly teach nurses and interns. We address district medical societies and lay organizations. Whatever the reason or combination of reasons, our highest rate of 10.4 in 1932 has not been exceeded.

There are three problems to be considered in controlling diabetes. (1) Can we prevent its development? (2) When it develops can we find it early? (3) Whether we find it early or late can we control the disease so that the patient has a normal life?

Can we prevent its development? Dr. Reginald Fitz of Boston in a recent article on "The prevention of diabetes mellitus" says "peculiarly little is known of the cause of diabetes. Certainly to find an assured organic basis for the disorder is by no means easy". He refers to recent work by Houssay and by Young which throws reasonable doubt on the belief that the pancreas primarily needs to be at fault in diabetes. Dr. Young showed slides recently from a diabetic animal which had developed a fatal diabetes although the pancreas had been left untouched. The disease was induced by injections of extract from the anterior lobe of the pituitary gland. The resultant changes that took place secondary to such treatment were indeed remarkable. Best has also done work along these lines.

Joslin says that heredity is the basis of the disease. White and Pincus, in interesting arguments, say that it is inherited as a recessive characteristic; Perkins regards the inherited tendency as dominant. But if diabetes were transmitted as a dominant trait eventually one parent of each diabetic would be diabetic. Thirty-five per cent of my cases have diabetic relatives; 20 per cent of Joslin's cases have diabetic relatives.

Admit, if you wish, that the tendency to develop it is inherited. What activates the diabetic gene? One of my diabetic female patients whose father died of diabetes had thirteen children; so far two of these adolescent boys have developed diabetes at a younger age than their mother or their grandfather. Another pair of patients, husband and wife, are both diabetics; they have 15 children and 2 of their boys have diabetes. Both these children developed it at a much younger age than the parents.

There are two stages of life when one is apt to develop diabetes. One during adolescence. Here boys outnumber girls, probably due to overactivity of the pituitary. The second great age is between 50 and 60, where women outnumber men, and obesity would seem to be the exciting factor. Joslin blames obesity. And obesity would seem to be guilty. It is rare to find a middle-aged diabetic who has not been over-fat at some time.

Now what can be done about prevention? Joslin says those with the diabetic taint should not marry others with it. But the disease develops so late in life that parents commonly develop it after at least some of their children are married. In my opinion any effort to regulate marriages is pretty futile. One of my girl patients, aged 17, who has eleven diabetic relatives, married a boy who also has some distant diabetic relatives. They had a baby within the year which is normal so far. There are worse things in life than having a diabetic child! Diabetics are clever, and diabetic children subject early to discipline make good citizens.

The other attack on prevention is urging the relatives of diabetics to keep their weight down. This may be done among high-grade intelligent people. Most of us find it hard enough to keep our own weight down, let alone that of our patients' relatives.

Can we find the cases early? We urge all our patients to test their immediate relatives, *i.e.*, parents, siblings and children. It is gratifying to send a patient home with a bottle of

Benedict's and have him bring back a diabetic relative!

Insurance examinations pick up more men than women; married women do not bother much about insurance, and single older women rarely have diabetes. Recently army tests have picked up a few early diabetics. Three young men have been sent to me from the Air Force, one of these had a renal glycosuria; the other two were true diabetics; none had symptoms.

Routine pre-natal urinalyses discover glycosurias which may turn out to be true diabetes. But we are not getting the fat middle-aged diabetic women early enough. More propaganda among club women is needed, among those middle-aged women who have been too fat ever since the last baby was born. If you start preaching control of diet they think you are just trying to take away one of their chief pleasures.

The average Canadian woman who does her own housework no sooner gets the dishes washed after one meal than she has to begin thinking about the next. Food is a very important part of her life. After feeding her family one of her chief recreations is attending teas in other people's homes. Dressing up the dining table with candles and flowers, crocheted table cloth, and delicious looking cakes is the great Canadian winter sport. The doctor who cuts this out of a woman's life, not because she has diabetes but because her great aunt had it, must be very convincing! And the woman who listens to the doctor will have to face social unpopularity; no hostess wants to slave half a day on a sugar and whipped cream confection only to have her guests say "No thank you". These afternoon teas are to the women what stag poker parties are to the men, an institution not to be lightly interfered with.

The patient who is reducing her weight tires easily and becomes irritable. True, after she gets the 25 pounds off she feels better, but there is no use pretending that reducing is anything but hard to accomplish.

A further source of new diabetics will be the children of those young diabetics who formerly died but have been saved by insulin. A diabetic aged 12 when insulin was discovered is now 30 and in the active reproductive age. In 50 years' time or sooner his children may swell the numbers of the diabetics.

Thirdly, can we give the diabetic a normal life? It can be almost normal when the general treatment of diabetes throughout the Dominion is as good as it can be. Considering the contribution Canadian scientists have made in this field Canadian clinicians as a whole have lagged far behind them.

From an aeronautical standpoint Regina is said to be the middle of the hemisphere. Be that as it may, we are in the centre of Canada as to sources of interns. We get them from every medical school in the Dominion, not A.O.A.'s but a good average type, the kind that the bulk of our population will be relying on for medical care the next 25 years. What do they know about diabetes? A hazy little! Canadian clinical teaching leaves a patchwork on the mind of the student. Every intern knows there has been argument as to high or low fat diets, and they all are prepared to give 100 units of insulin to every unconscious diabetic patient arriving at the hospital, which is not so good if the patient is in a hypoglycæmic reaction.

Any disease that is tenth in the causes of death and which is increasing and will be likely to increase deserves more time and care in the medical curriculum. Work with diabetics is fussy and time-consuming; they need so much conversational treatment; but there are few intellectual or technical problems in the care of the diabetic—nothing that the average medical student could not easily absorb. The average young physician should be doing his own blood sugars even as he does his own white counts. Doing a blood sugar is far easier than making a cake. The undergraduate should be given enough practice at it not to feel it is a big undertaking. Some of my patients learn to do their own just for a hobby. Figuring the diet is another bugbear, overcome either by a few hours' practice or by giving unweighed moderate diets.

Some of us are so afraid of dogmatism, so fearful of giving the student a fixed idea, thus blighting his inquiring scientific outlook, that we give him no clear ideas at all. No matter what specialty the young physician chooses he cannot get away from the diabetic. The oculist sees diabetic cataracts and retinitis, the orthopædist deals with gangrene and diabetes-exciting fractures; the obstetrician must decide whether or not the diabetic mother needs a Cæsarean section; the genito-urinary man can try to clear up those too prevalent kidney infections; the cardiologist can watch those hypertension people; the surgeon can see his hyperthyroids

become true diabetics; the chest man can get his tuberculous diabetics out of the sanatorium faster if he keeps their blood sugars normal; all these specialists need a good grounding in the principles of the disease.

Suppose this medical millenium to have taken place, and every diabetic is getting the best possible medical care, what does life hold for him? The middle-aged diabetic who makes up the majority of patients is not a very difficult problem. Give these people enough to eat and insulin to keep them sugar-free or nearly so and they have a pretty good life. The complications which overtake them when they do not follow the rules are distressing; diabetic retinitis, cataract, gangrene, hypertension and all its evil train. A question which can be discussed for hours is, which comes first, diabetes or arteriosclerosis?

Six-year old patient taking her own insulin.

Sooner or later all elderly diabetics have arteriosclerosis, possibly they have it sooner than the non-diabetic population.

What about the young diabetics? They are the ones who require good treatment *now*, not the year after next. They must grow, and they must not be subject to infections or liable to reactions. Protamine zinc insulin has made life much pleasanter for them.

Some of my early patients who were very co-operative and tried very hard to keep sugar-free, mostly cases who required four doses of the unmodified insulin, became very liable to reactions; they became sensitive to an extra unit or so of insulin, to a change in temperature if the weather turned suddenly warm, or to extra exercise. One boy who is highly intelligent and very co-operative varies from glycosuria to reactions from hour to hour. These are the most difficult diabetics to treat. Their blood sugars vacillate so much that even confining them to hospital for study sends up the blood sugar and insulin requirements. They seem hypersensitive to any stimulus. One of these boys told me that if he is showing sugar at 11 a.m. and eats some carbohydrate he is sugar-free by noon but if he eats nothing he still has sugar by noon. This is in line with Best's work on carbohydrate diets producing more insulin in the pancreas. Protamine zinc insulin has been a help to this boy, but he cannot allow himself to forget for four hours that he is a diabetic. Blood sugars in these cases are subject to tremendous oscillations during a 24-hour period.

We would all like to keep our young diabetics with blood sugars between 70 and 170, but if they have to run the risk of reactions to be kept there let them have a high blood sugar once a day. Does this blood sugar over 200 once a day favour or hasten the development of vascular sclerosis? No one really knows. Even if it did, it is better than scaring the wits out of the family by having the patient fall unconscious and go into convulsions without warning. Since the use of protamine zinc insulin the onset of a reaction is more insidious. Very often the patient becomes unconscious without warning. I have observed blood sugars much lower without symptoms than when using unmodified insulin. In two cases I found blood sugars of 25 mg., taken while the patient was in the office at noon, without symptoms.

Maintain a normal blood sugar 24 hours a day if you can, but if it is a choice between a normal blood sugar and reactions or a high blood sugar for a quarter of the day and no reactions there is no question as to the choice. There must not be reactions.

The adolescent may feel all right but he may be showing from 1 to 3 per cent sugar all the time. This is the one who does not grow. Everyone strives for eternal youth, but a diabetic aged 20 who looks 15 is just a tragedy. One sees occasional diabetic dwarfs. Their parents had them put on a diet at 8 or 10 years of age, and

have kept them on the same diet ever since, even if they are now 15 or 16. One has to get busy on these children and impress on their parents that they have only so long to grow, and that when their epiphyses close growth is over. One such boy, aged 16 was worried about being short; he was on diet and insulin but showing about 2 per cent sugar all day. When he was rendered sugar-free he grew five inches in a year.

It would not be orthodox to close this paper without mentioning high fat or high carbohydrate diets. I let the older people have about what they like, four slices of bread a day and a potato at noon, butter enough to keep their meals from being too dry. They aren't fussy about a lot of meat, especially the women.

We have done some experiments on the young. We give them a high carbohydrate diet, take blood sugars at 10 p.m. and 8 a.m., then note the rate of fall, then give them a diet worth the same calories, but high in fat and low in carbohydrate. The blood sugars fell less rapidly. We thought this was due to the fact that fat is absorbed more slowly than is the carbohydrate.

They don't care for either extreme, so we compromise and give the 15 year old boy who is so hard to fill, about 100 P., 130 F. and 250 C.,

TABLE VI.

90 P. – 90 F. – 350 C.	
(60) 20 insulin	
Blood sugar 10 p.m.	363
8 a.m.	125
Difference	238
Rate of fall per hr.	23.8 mg.
90 P. – 160 F. – 125 C.	
(60) 20 insulin	
Blood sugar 10 p.m.	119
8 a.m.	47
Difference	72
Rate of fall per hr.	7.2 mg.

TABLE VII.

BLOOD SUGARS

	High C.	*High fat*
8 a.m.	125	62
11 a.m.	55	54
2 p.m.	364	153
6 p.m.	142	84
10 p.m.	339	119
8 a.m.	87	47

approximately 2,600 calories. That seems to keep his mind away from his stomach and make him contented.

A word as to occupations for the diabetics. Many of my boys are farmers. This is an irregular life, long hours part of the year and not much to do in winter. A business with regular hours is good. Medicine is not very good; one of my patients planned to be a pædiatrician but changed to be an anæsthetist, which suits him better. Some are teachers. The girls are nurses and teachers.

I tell the diabetic boys, now that their contemporaries will be decimated by war, it is up to them to get a good education and be prepared to help run the country.

RÉSUMÉ

Le taux de mortalité du diabète au Canada, qui était de 12.1 en 1933 passa en 1937 à 14. Ontario a le pourcentage le plus élevé tandis que la Saskatchewan a le plus bas. Le genre de vie est un facteur assez discutable comme agent provocateur du diabète. Le diabète est une affection souvent héréditaire. La lutte contre l'obésité est une excellente prophylaxie du diabète. Il faut examiner systématiquement les urines des proches parents de diabétiques. Il semble que cette maladie n'est pas suffisamment comprise des étudiants en médecine et que l'on n'insiste pas assez sur ses aspects divers. Tous les spécialistes rencontrent des diabétiques; ils ne devraient donc rien ignorer du diabète, au moins dans son ensemble. Le jeune diabétique peut maintenant envisager la vie avec confiance grâce à l'insuline-protamine-zinc qui diminue et retarde les réactions. La combinaisons des régimes graisses-hydrocarbonés varie à l'infini et doit s'adapter à l'individu traité. Quant au genre de vie des diabétiques, il peut varier selon les tempéraments à condition de ne rien sacrifier aux règles permanentes qui régissent leur singulier dérèglement.

J. SAUCIER

A curious anecdote of Jacob Bobart, keeper of the physic garden at Oxford, occurs in one of Grey's notes to *Hudibras*—"He made a dead rat resemble the common picture of dragons by altering its head and tail, and thrusting in taper sharp sticks, which distended the skin on each side till it resembled wings. He let it dry as hard as possible. The learned immediately pronounced it a dragon; and one of them sent an accurate description of it to Dr. Magliabecchi, librarian to the Grand Duke of Tuscany; several fine copies of verses were wrote on so rare a subject; but at last Mr. Bobart owned the cheat. However, it was looked upon as a masterpiece of the art; and as such deposited in the Museum."—William Wadd.

PERIODIC FLUCTUATIONS IN THE BLOOD PICTURE IN CANCER AND THEIR BEARING ON RADIATION THERAPY*

BY O. C. GRUNER, M.D.

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WHEN a patient is undergoing treatment for cancer, a repeated study of the blood shows changes of varying intensity. The blood picture may be apparently quite normal soon after a course of radiation, only to become abnormal again later, even preceding the clinical appearance of metastasis.

At first sight it is only to be expected that the initial improvement should occur after removal of a neoplasm, or after radium or x-ray therapy, while the later change may be the result of action on the blood-forming organs. However, a careful analysis of some 400 cases so far examined in the Tumour Clinic of the Montreal General Hospital has shown that the relation between clinical progress and quality of blood picture is not at all simple. In 144 of these cases observations have been made over a sufficiently long period to show that the events after treatment fall into such groups as the following.

TABLE I.

No. of cases	*Clinical course*	*Blood picture*
25	Apparently cured	Continuously normal
31	" "	Persistent slight abnormality
9	" "	Steady worsening
15	Metastasis later	Persistently abnormal
38	Progressive worsening	Progressive worsening
15	Stationary	Stationary
11	Advanced disease	Absence of inclusion bodies

It is necessary to assess the degree of blood change in the blood picture in order to investigate these groups. This is done on the basis mainly of easily obtained data: the number of monocytes, the number of small lymphocytes, the percentage of leucocytes whose nuclei have "bizarre" contour, the presence of mitochondrial inclusions in the monocytes. Four grades are defined, as stated in a previous communication.[1] An abridgement is submitted for convenience. See Table II.

The correlation of the clinical course with the blood picture is very clearly shown when the two series of data are combined into one graph. This is now done for every patient as soon as more than two blood tests have been made. The accompanying figures illustrate the method. The horizontal lines show the blood grade found at each successive attendance of the patient. The vertical lines mark off the time-periods. The space above the grade lines is used for recording the essential clinical notes and the dates of treatment. The space below is used for entering one or two useful details found in the blood count.

The time periods marked off in red lines have been inserted since studying the observations on periodicity in cancer published by Douglas Webster.[2] Careful statistical analysis of the clinical features in 820 cases led him to formulate a 33-week period. In applying this to the present series, the date of commencement of treatment was chosen as a starting point because the laboratory protocols only specified the dates of operation or radiation, the original object of the work having been to correlate blood reaction to the different types of therapy adopted for various sites of cancer.

The subsequent events in the history have been found to fit in with this periodicity to a striking extent in very many cases. Thus, in every one of twenty-eight cases in which re-

* This work was made possible by a grant from the Archibald Cancer Research Fund, McGill University, Montreal.

TABLE II.

GRADES OF BLOOD PICTURE

Grade	*Monocytes percentage*	*Leucocytes per c.mm.*	*Lymphocytes percentage*	*Bizarre nuclei*	*Inclusion bodies*
1	8	About 5,000	About 15	Few	Very few
3	12 to 20	" 10,000	5 to 8	Many	Numerous
4	Over 20	Up to 12,000	Absent	Many	Easily found. Includes mycelial forms

Grade 2 shows characters intermediate between those given for 1 and 3.

peated exacerbations are evidenced by a record of additional surgical or radiological intervention, the dates of these follow the cycle with exactitude. In the example shown in Fig. 2 the radium applications could hardly have fallen in with the peaks of the cycles more exactly had the surgeon deliberately calculated out the dates on which to do them.

In eight cases where there was a long interval of time between the primary and secondary lesions the latter appeared at the calculated date. In one of these, 27 cycles had been passed before the secondary appeared. In another, a case of mammary cancer in a male, the first operation was done in London, Eng., twenty-seven years before an operation was necessary for the development of a growth in the other breast. The second operation in Montreal was done at a time corresponding to the calculated date. In a third case, one of sarcoma, the first operation was done in Vancouver, the second was done four years later in Montreal, the third five years later in Kingston, and a fourth was done seven years later, again in Montreal. The date of each event fitted in with the calculated cycles.

Again in 34 out of 36 fatal cases, the date of death coincided with the red line on the graph. An example is given in Fig. 4. Fifteen of these cases ran in half-cycles, and the length of life was ½ cycle in one, 1 cycle in one, 2 cycles in seven, and 3 cycles in six cases. This confirms Webster's finding that the half-cycle cases have a bad prognosis. One case had run through 12 cycles before the fatal result occurred, and yet the date of death fell on the calculated day.

When the graphs are now studied in regard to the behaviour of the blood grade during these periods, a rise and fall can be seen as the disease waxes and wanes, being often lower in the middle period and high at the end. Thus, in Fig. 2 there is a fall in the middle of the third and sixth cycles and a peak at the end of the first and fourth. The behaviour is not absolutely consistent in every case, for many show a temporary fall soon after the radiation and remain almost continuously high at other times. This applies not only to the blood grade as a whole but also to the presence of the inclusion bodies, for these are implied whenever the curve rises to three degrees or higher.

An attempt was made to determine how the individual varieties of inclusions behave during a period. For this purpose it has been found

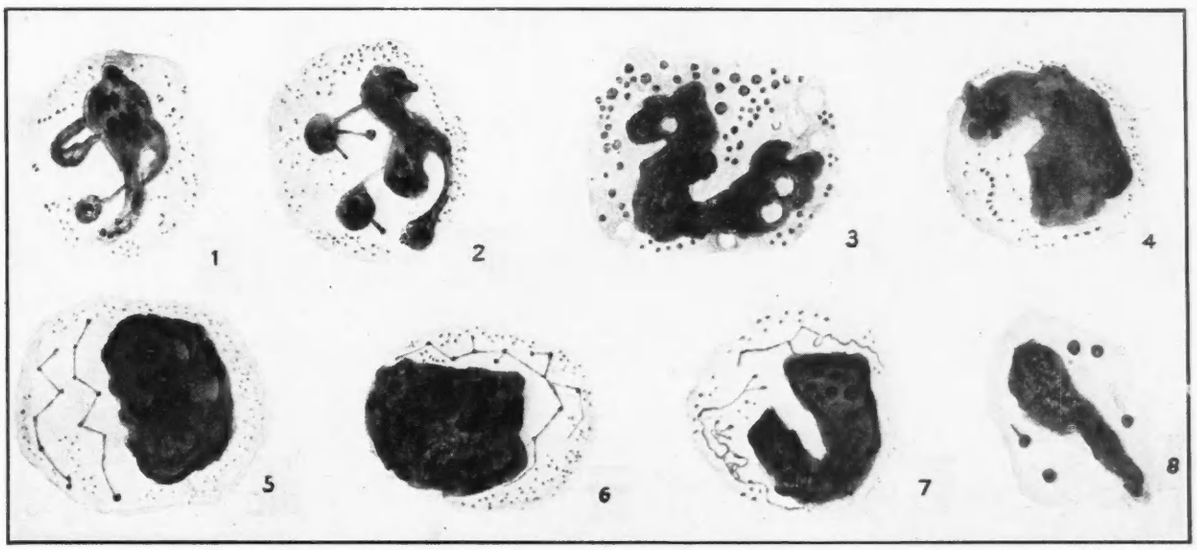

Fig. 1.—Abnormal leucocytes in the blood in cancer: 1, 2, bizarre polymorphonuclears; 3, bizarre monocyte showing numerous round (azurophile) inclusions and vacuoles in the nucleus; 4, monocyte with two "thrix" forms of inclusions; 5 and 6, monocytes with "geniculate" bodies; 7, monocyte with "mycelial" form of inclusion; 8, monocyte with five large round forms of inclusion.

As regards the mitochondrial inclusions which were first described in 1917, and again in 1934,[3] Fig. 1 depicts four varieties* which are commonly found in the blood monocytes of cancer patients (*a*) "geniculate" forms; these show angular filaments, with azurophile thickenings at each node; (*b*) "thrix" forms — beaded or barred forms; (*c*) "mycelial" forms — these are collections of short beaded filaments which are interwoven like an early mycelium; (*d*) globular azurophile bodies similar to those called "virus bodies" when found in the tissue cells in certain virus diseases. All these inclusions are stained red with Leishman's stain. They occur in every 10th to 12th monocyte in grade 3 blood and every 4th to 6th in grade 4.

* These are recorded by code numbers on the protocols (31, 32, 50, and 80 respectively).

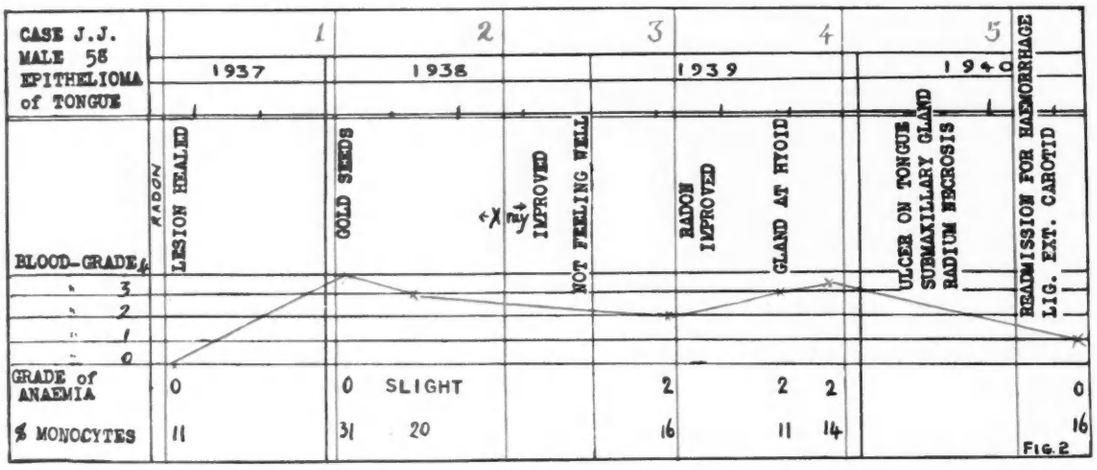

FIG. 2

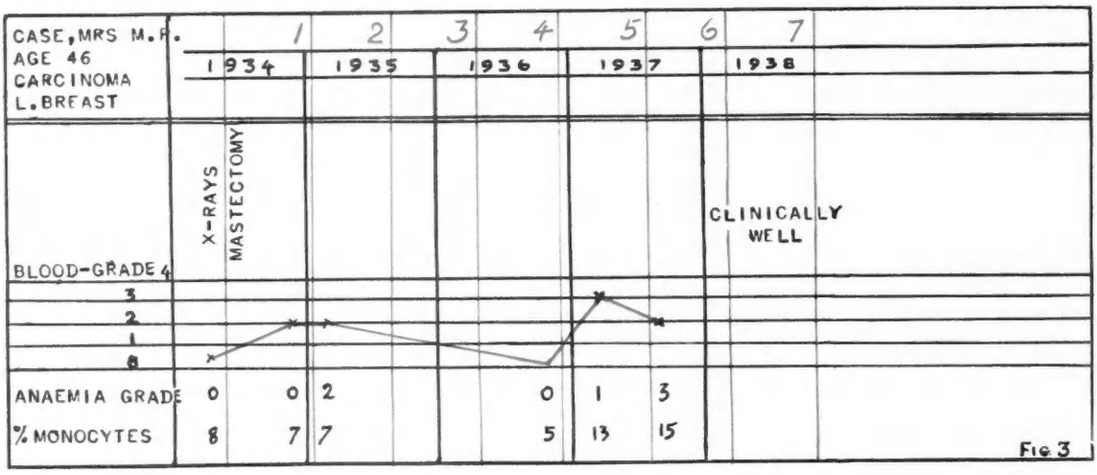

FIG. 3

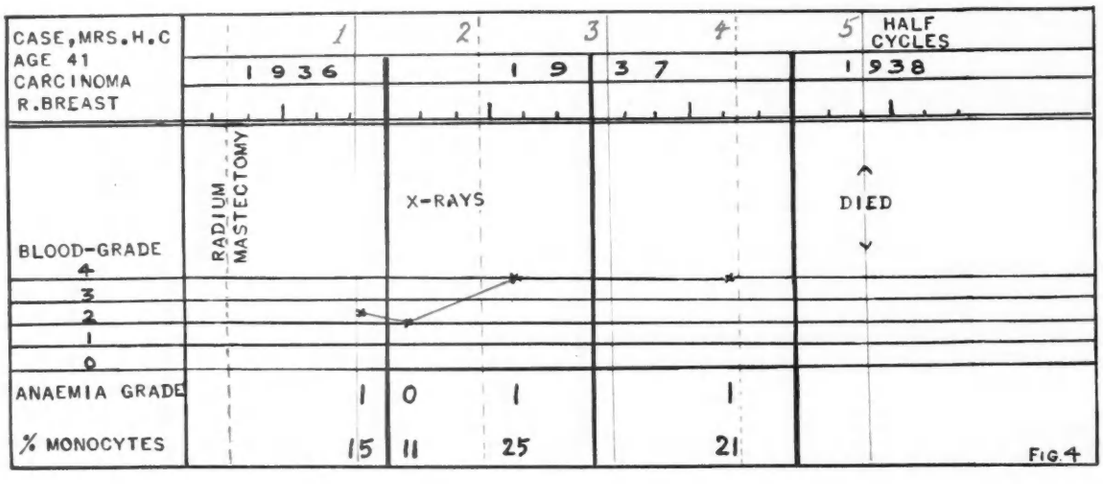

FIG. 4

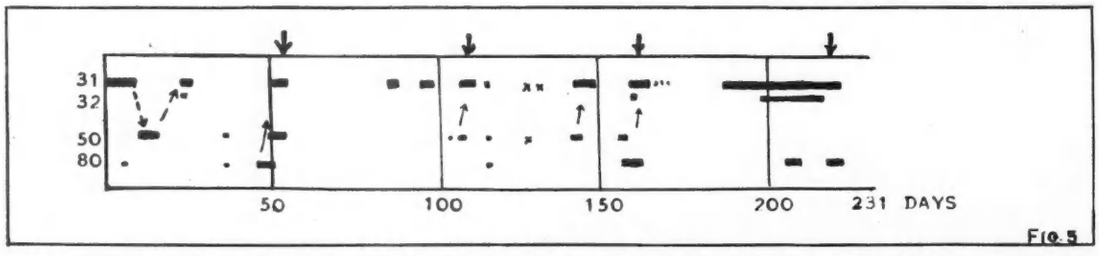

FIG. 5

Fig. 2.—Graph from a case of cancer of the tongue showing the relation of the clinical features and the changes in the blood picture to the 231-day period. The red lines mark off these periods. **Fig. 3.**—Graph from a case of cancer of the breast which has remained clinically free of disease for nine cycles. **Fig. 4.**—Graph from a fatal case running its course in five half-cycles. **Fig. 5.**—Distribution of the chief kinds of inclusions in the leucocytes day by day through the cycle—"31": geniculate forms; "32": "thrix" forms; "50": "mycelial" forms; "80": "virus bodies". The graph shows four periods during which they are not seen.

best to reckon in days (231-day cycle). Each of the several hundred blood-count protocols worked out for this Clinic has been re-dated according to the day of the cycle determined for each patient. A chart long enough to accommodate a 231-day baseline was filled in with the types of inclusion body noted on each protocol, expressed by their code number.* This analysis has shown that some of the types are not continuously present. The "geniculate", "thrix", and "mycelial" forms appear between the 48th and 54th day, between the 105th and 115th days, between the 154th and 165th days, and finally between the 212th and 226th days. The first of these three appear to precede the second, and the third appears last. The round azurophile intracytoplasmic forms precede the geniculate forms at two points, namely the first and third parts of the cycle (Fig. 5). Should systematically extended observation in the future show that such variations are usual, they are strongly suggestive of the presence of an underlying exogenic factor which is periodically active. Cases which show half-cycles would be explained, as Webster suggests, by supposing two simultaneous "infections" on the analogy of mixed malarial infections. This would account for the bad prognosis and accelerated course of such cases. It remains to be seen whether there is a relation between these various forms in the leucocytes and those found in fresh tumour tissue[4] and in tissue cultures.

The following corollaries may be drawn. (1) The diagnosis of cancer from the blood (by whatever method studied—cystological, chemical, cultural, dark-field, or by crystallization) may be unsuccessful if the material was collected at a "negative" phase of the cycle. (2) The particular part of the cycle at which the patient stood on his first attendance at the clinic might also be determined from the inclusion-content of the blood as furnished by the blood-films. (3) The results of radiological treatment might be more successful if timed for a certain part of the cycle. Periodic examination of the blood from this point of view should be of much assistance. (4) Other chronic diseases might be advantageously studied from the standpoint of cyclical periods.

* The findings necessarily fall far short of statistical value, as no doubt 23,100 counts should be made, and at least 100 patients should be under daily observation at once, or 200, if tests are made on alternate days. So far, this number of cases has required several years to collect.

SUMMARY

A study of a series of cases attending the Tumour Clinic of the Montreal General Hospital has shown that in 87 out of 95 cases, the dates at which recurrences appear conform with the 33-week period in cancer brought forward by Douglas Webster.

Fluctuations in the blood grade show some relation to the same cycle although in many cases (77 out of 144) the grade remains continuously high whatever treatment is adopted. The inclusion bodies themselves were found oftener during four subdivisions (about 52 days) of the same cycle.

It would seem therefore that the 231-day period may be recommended for consideration both by the clinical pathologist and the radiologist.

Grateful acknowledgment is here made of indebtedness to Dr. C. K. P. Henry for the facilities of the Tumour Clinic at the Montreal General Hospital and for his continual encouragement in these researches.

In view of the close resemblance between the conclusions expressed in the present paper, and those particularized in a recent review of Webster's book in the *British Medical Journal*, it may be stated that the present results are those actually reached in our own cases without knowing of the details in the book.

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"That fatigue is a practical factor in the production of malnutrition today is unfortunately only too true. I have repeatedly condemned the practice of allowing children to be up and about, roaming the streets of this city, until 'all hours' at night. This is a social evil of the first magnitude, the ill-effects of which have been aggravated by the artificial prolongation of the hours during which children are out of bed. It is now, unfortunately, extremely difficult (if not impossible) under modern urban conditions to ensure sufficient sleep and rest for the children. The neighbours' wireless sets, the noise of traffic, the cries of other children in the street, the persistence of daylight, and numerous other factors all conspire to break the morale of the conscientious city mother who realizes the necessity of sufficient rest for her children and who may eventually find it easier to drift with the tide and to leave the health of her children to chance."—Dr. J. C. Saunders, M.O.H., Cork.

THE SIGNIFICANCE OF GALLOP RHYTHM*

BY F. CARLYLE HAMILTON, B.A., M.B.

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AUSCULTATION of the human heart customarily reveals two heart sounds. The first, usually best heard at the apex, is thought to be due to the closing of the mitral and tricuspid valves, although vibrations set up in the cardiac wall by ventricular contraction may be an additional factor. The second, loudest at the base of the heart, is assumed to be due to the closing of the semilunar valves. Convincing evidence supports these suppositions. When the heart sounds are recorded by various mechanical and amplifying devices, however, additional sounds, not readily audible to the human ear, may be found. Thus, McKee,[1] in a recent article, states that four heart sounds are normally recorded in school children.

Under certain circumstances three heart sounds are easily audible with an ordinary stethoscope. Probably every physician is able to recall such cases, but, to the majority, a satisfactory explanation of this phenomenon is not apparent. In describing three sounds for each cardiac cycle I am not referring to splitting of the first or second sound, nor to any type of murmur or cardiac friction sound.

The circumstances under which three distinct heart sounds are heard are two-fold: first, in children or young adults with normal hearts, in whom a third physiological heart sound is audible early in diastole; and second, true gallop rhythm, which forms the subject of this paper.

Physiological third heart sounds do not indicate disease; in fact they are found in the healthiest types of hearts, and in persons usually under twenty years of age. Exercise followed by the assumption of the left lateral decubitus position may make the third heart sound surprisingly loud. This third heart sound is thought to be due to vibrations set up in the relaxed ventricular walls by the sudden and forcible entry of blood from the auricles immediately after the opening of the auriculoventricular valves. If in such cases the rate of the heart is fast the sounds may be identical with gallop rhythm. The modern tendency is, however, to reserve the latter term for hearts showing actual disease.

Gallop rhythm is defined as the rapid repetition of three heart sounds with each cardiac cycle. To the ear there is a resemblance to the sounds associated with the galloping of a horse. While any such grouping of sounds originating in the heart might be termed gallop rhythm, it is again stressed that it would seem wise to reserve the term for pathological cases, in which gallop is an ominous sign, omitting entirely the younger group with normal hearts and loud third heart sounds. With rapid heart rate the latter group may present heart sounds indistinguishable from gallop, but obviously of no prognostic significance whatever. Such a view was suggested by Wolferth and Margolies,[3] in 1933. It allows us to include gallop rhythm among the other important signs of serious heart disease, such as cardiac enlargement, diastolic murmurs, auricular fibrillation, etc.

In the literature many attempts have been made to classify gallop rhythm. There is a type caused by a third sound during systole; this is rare and apparently not of much significance. The common variety is diastolic gallop rhythm. In this type the abnormal third sound occurs in diastole either early, or late, or in the mid-portion of diastole. In the early diastolic type the timing of the third sound is identical with that already described for the physiological third heart sound. This has been termed proto-diastolic gallop rhythm. Here, the explanation of the abnormal third sound is not difficult. We know that at this particular instant in the cardiac cycle the valves separating auricles and ventricles have just opened, and that the pressure in the well-filled auricles is high relative to that in the relaxed ventricles. Add to this a pathological condition of the wall of the ventricles in which there is poor muscle tone accompanied by abnormal dilatation of the ventricular cavity, and we have the circumstances which apparently create not only the third sound

* Read at the Seventy-first Annual Meeting of the Canadian Medical Association, Section of Medicine, Toronto, June 21st, 1940.

From the Department of Medicine, University of Toronto, and the Toronto Western Hospital.

responsible for gallop, but also the palpable apical impulse which accompanies this sound.

If the third sound occurs late in diastole the gallop is termed presystolic. In this case the explanation is equally simple. Auricular systole sends a quantity of blood into the ventricles, which, as above described, have previously lost their customary tone. Whether the third sound occurs early or late in diastole will depend on the time at which blood enters the ventricles under greatest impetus. That a sound and palpable shock occur at all is dependent on the abnormal condition of the ventricular wall due to previous cardiac disease. Occasionally both protodiastolic and presystolic elements may be present in the same cardiac cycle, and may be recorded as such in a phonocardiogram. Under this circumstance, if the heart rate increases, summation of these two elements will occur, producing a diastolic third sound in the middle of diastole. This was formerly termed mid-diastolic gallop, but latterly has been referred to as the summation type. It should be added that gallop rhythm is usually best heard either at the apex or somewhat medial to the apex.

During the past two and a half years we have recorded phonocardiograms of 32 cases of diastolic gallop rhythm. This does not signify that only 32 cases have been encountered. There have been many others in which the recording of the heart sounds could not be conveniently done, and still others where recordings were made but failed to show clearly what the ear had heard. The instrument used was the Cambridge stethograph attached to a mobile unit of the Cambridge electrocardiograph. While it has been

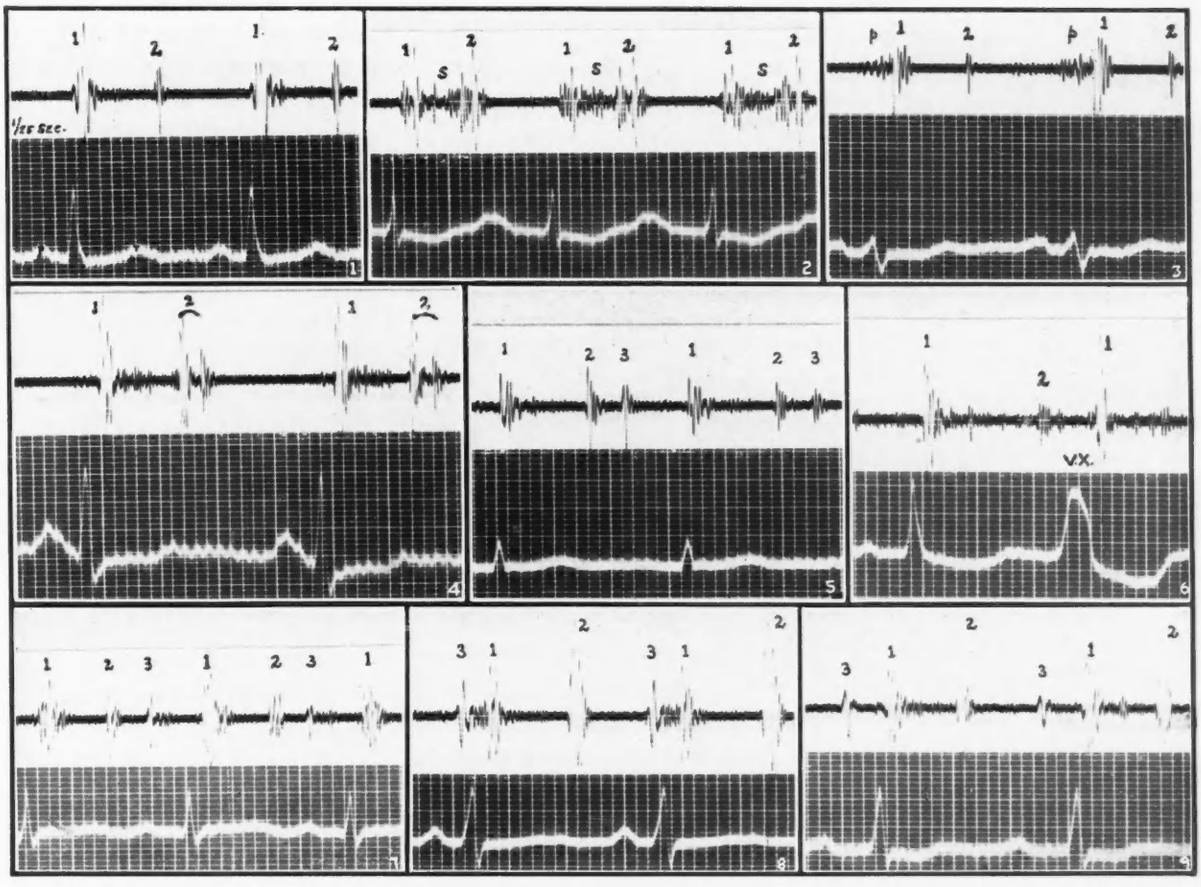

Fig. 1.—Normal heart sounds. Note that the first sound occurs toward the end of the QRS complex of the electrocardiogram, and that the second sound is immediately at the end of the T-wave. **Fig. 2.**—Systolic murmur (s). **Fig. 3.**—Presystolic murmur (p). **Fig. 4.**—Splitting of second heart sound. **Fig. 5.**—Physiological third heart sound in a young individual with a normal heart. Heart rate 90. **Fig. 6.**—Normal beat followed by a frustrate extrasystole; this sequence might be misinterpreted as a slow gallop. **Fig. 7.**—Protodiastolic gallop rhythm. Heart rate 107. The third heart sound occurs at the summit of the P-wave, too early to be associated with auricular activity. **Fig. 8.**—Presystolic gallop rhythm. Heart rate 91. The third sound occurs too late after the previous second sound to be considered "protodiastolic". It commences 0.13 seconds after commencement of the corresponding P-wave of the electrocardiogram. **Fig. 9.**—Presystolic gallop rhythm. Heart rate 88. Third sound commences 0.12 seconds after commencement of corresponding P-wave. The increased distance between the third and next first heart sound is explained by delayed conduction in the electrocardiogram (PR 0.24 sec.).

stated by Orias and Braun-Menendez[2] that a jugular tracing is much superior to an electrocardiogram in timing the events in the phonocardiogram the electrocardiogram is none the less helpful.

Of our 32 cases of gallop rhythm, 18 were males and 14 females, chosen mainly from the public wards of the Toronto Western Hospital. In Table I is shown the number of patients in each age-group, and the number at present living and deceased. Gallop rhythm was found only once under 30 years of age; this was in a male, aged 22 years, who entered hospital in failure, with an enlarged left ventricle associated with well-marked coarctation of the aorta, and a blood pressure in the arm of 200/130.

TABLE I.

Age groups	*Number of cases*	*Number living*	*Number dead*	*Number untraced*
20-29....	1	1	0	0
30-39....	8	2	6	0
40-49....	1	1	0	0
50-59....	11	8	3	0
60-69....	6	2	2	2
70-79....	4	2	2	0
80-89....	1	1	0	0
Total..	32	17	13	2

It will be noted that the mortality was unusually high in patients showing gallop rhythm in the fourth decade of life; 6 of the 8 patients in this group died, at an average interval of three weeks after the recording of the stethogram. Of these 2 had chronic nephritis with hypertension, 2 had malignant hypertension, in 1 rheumatic heart disease was responsible, and in 1 there was hypertension with terminal coronary thrombosis. Of the two survivors 1 has been under observation with chronic nephritis and hypertension during two years' time, and the other, with rheumatic heart disease and hyperthyroidism, has responded well to thyroidectomy.

In the 23 patients who were over 40 years of age the cardiac etiology and the result of treatment is shown in Table II. The mortality in this group has been lower than was anticipated. Of these 23 patients, only 7 are known to have died (at an average interval of 11 weeks after sound recording), although 2 others have not been traced.

Post-mortem examination was made in 4 of the 13 fatal cases. The weight of the heart in these 4 cases was 310, 400, 520 and 550 g. respectively. In each, there was left ventricu-

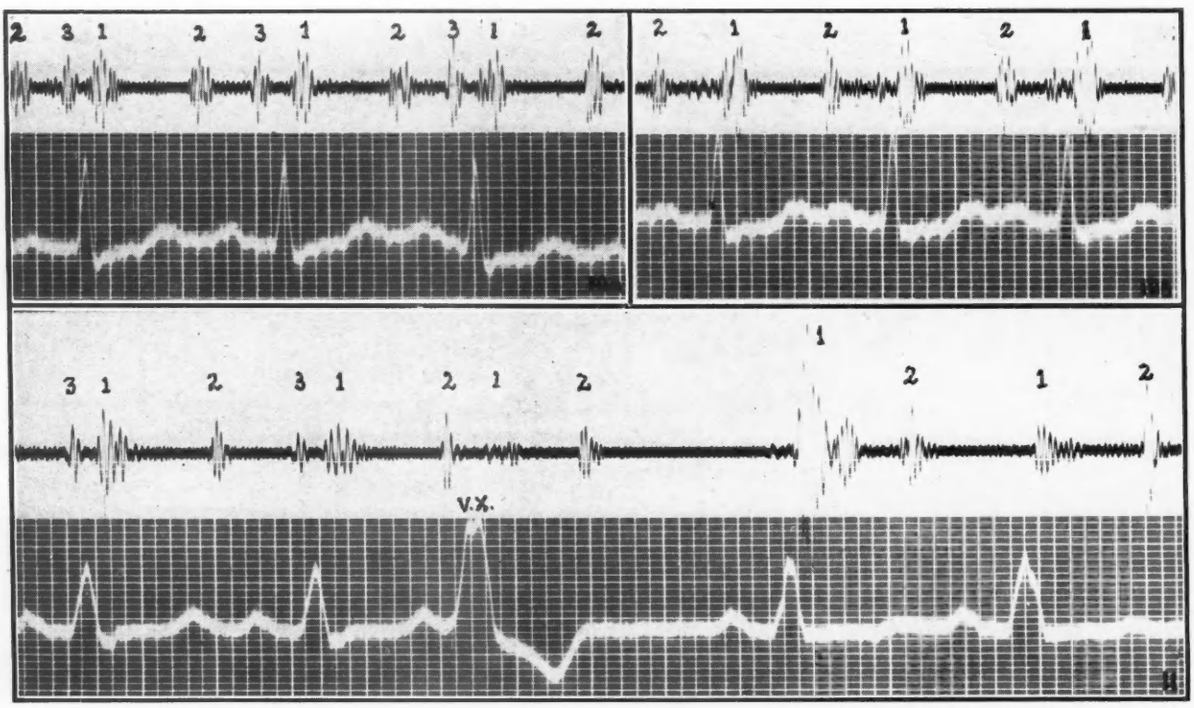

Fig. 10A.—Summation gallop is shown. Heart rate 115. Third sound in mid-diastole. The summation is due to the superimposition of protodiastolic and presystolic elements, which separately register poorly in stethogram and which were inaudible to the ear, although gallop was easily heard in this case when the heart rate was 115. **Fig. 10B.**—The heart rate has increased to 126, and the gallop has practically disappeared. **Fig. 11.**—Presystolic gallop, which disappeared for several beats after a ventricular extrasystole (VX). Heart rate 104.

TABLE II.

GALLOP RHYTHM—GROUP AGES 40 TO 89 YEARS

Etiology	*Number living*	*Number dead*	*Number untraced*	*Total*
Hypertension with coronary sclerosis...	9	5	1	15
Hypertension without coronary sclerosis...	3	0	0	3
Coronary sclerosis without hypertension.....	2	2	1	5
Total.....	14	7	2	23

lar hypertrophy. These 4 cases were all from the fourth decade. One showed rheumatic heart disease; 1, acute nephritis; 1, chronic nephritis; and 1, advanced nephro-sclerosis; none of these showed marked coronary sclerosis.

Of the 32 cases in this series, 25 had definite hypertension, the systolic range being from 160 to 280 mm., and the diastolic from 100 to 200 mm. In some of the remaining 7 cases previous hypertension may have been a factor without our knowledge. In 29 of the 32 cases cardiac enlargement, proved by x-ray examination in all doubtful cases, was present. In 2 the size of the heart was normal. In one case no record of heart size was available. In 29 definite electrocardiographic abnormalities were present, and in 3 the electrocardiogram was normal. Without exception, all cases had serious heart disease.

Table III shows the heart rate in cases presented. It will be noted that in 27 of these 32 cases of gallop rhythm, the heart rate was between 90 and 130. In only 2 of our series, was auricular fibrillation present; and as would be expected these showed the protodiastolic type of gallop.

TABLE III.

Heart rate per minute	*Number of cases*
Under 90.....	4
90 to 99.....	3
100-109.....	14
110-119.....	6
120-129.....	4
Over 130.....	1
Total.....	32

In many instances it is difficult to determine the type of gallop even after examining the tracings, for the rapid heart rate usually present reduces the length of diastole to such a degree that the third sound tends to take up a mid-position in diastole. In so far as careful study would reveal, protodiastolic gallop was found in 11 cases, presystolic in 9, summation in 10, and

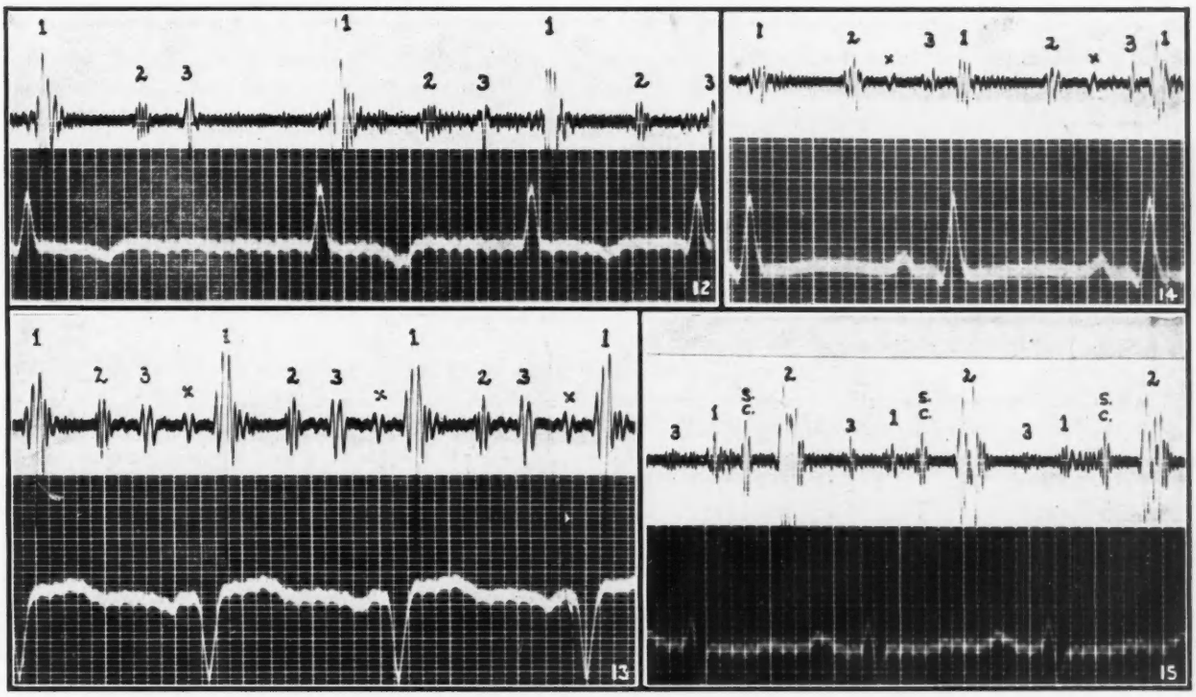

Fig. 12.—Protodiastolic gallop rhythm in a case with auricular fibrillation. Heart rate 100. Note the varying interval between third and following first sound. **Fig. 13.**—Protodiastolic gallop, in which an inaudible presystolic element is recorded (x). **Fig. 14.**—Presystolic gallop, in which an inaudible protodiastolic element is recorded (x). **Fig. 15.**—Probable presystolic gallop in which a systolic "click" was also audible. This patient had four audible heart sounds for each cardiac cycle.

in 2 cases the type was uncertain. In other words, the three types of diastolic gallop were found in approximately equal numbers. The prognosis was least favourable in the protodiastolic type, as shown in Table IV.

TABLE IV.

Type of gallop rhythm	*Number living*	*Number dead*	*Number untraced*	*Total*
Presystolic	6	3	0	9
Protodiastolic	4	7	0	11
Summation	5	3	2	10
Uncertain	2	0	0	2
Total	17	13	2	32

A number of illustrative phonocardiograms are shown. Figs. 1 to 6 show normal heart sounds, murmurs, splitting of heart sounds, physiological third heart sounds, and false gallop created by a "frustrate" ventricular extrasystole. Figs. 7 to 15 show phonocardiograms selected from the present series of 32 cases of gallop rhythm, to demonstrate the various points already mentioned in this article. The footnotes are self-explanatory.

The treatment of patients with gallop rhythm is that of the underlying heart condition. Practically all of our series required prolonged rest in bed because of myocardial failure or because of recent coronary thrombosis. Several had alarming degrees of hypertension, and others required treatment for kidney failure. The majority were given digitalis to improve myocardial contraction and lessen ventricular dilatation. Mercurial diuretics were used in the majority with congestive failure. In many cases the gallop disappeared after a few or several days' treatment. In others it persisted, and was later heard at heart clinic when the patient was again moderately active. In other words, the cardiac function, and not the occurrence of gallop, must decide the necessity for treatment.

CONCLUSIONS

1. Gallop rhythm is a fairly common and easily recognizable sign of serious heart disease. It must not be confused with the rhythm created by a third physiological heart sound.

2. Gallop rhythm occurs chiefly in connection with long-standing hypertension. It is always associated with serious heart disease.

3. The three types of diastolic gallop occur with equal frequency. The protodiastolic type has the most serious outlook.

4. Some evidence is presented to suggest that the prognosis is most serious when gallop rhythm occurs during the fourth decade of life, since many of these cases result from hypertension secondary to chronic nephritis or from malignant hypertension.

5. In older patients with gallop rhythm the immediate prognosis was found to be somewhat better than anticipated, which should encourage us to treat thoroughly the underlying heart condition in all such cases.

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The kind of food eaten by patients being treated with sulfanilamide may have an important bearing on the results of the treatment and whether or not the sulfanilamide causes toxic effects. If the patients get too little protein food, such as meat, eggs and milk, they may be more likely to experience toxic effects from the drug, but the drug may be more effective because of reaching higher concentrations in the blood when the dietary protein is low, it appears. Rats were the patients in the National Institute of Health studies. A low protein diet (7 per cent protein) increased their susceptibility to sulfanilamide "by increasing the mortality rate and the incidence of anæmia as compared with similarly treated rats on a diet containing 30 per cent protein". The concentration of the drug in the blood was somewhat higher in the rats on the low protein diet which "may possibly account for the greater toxicity. "This also raises the interesting question as to whether this might not be more than offset by the obvious advantages of higher concentrations of blood sulfanilamide in the therapeutic (remedial) application of the drug."—*Science News Letter*, February 1, 1941.

THE DIFFERENTIAL DIAGNOSIS OF UROLOGICAL CONDITIONS FROM ABDOMINAL LESIONS*

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THE painful stimuli from kidneys and ureters is referred to and gives tenderness in the superficial areas of the body which receive their sensory innervation through the same spinal segments. The painful area is narrower near the vertebræ and spreads out fan-wise towards the mid-line. This is partly due to the plexus formation and interconnections found between branches of the 10th dorsal to 1st lumbar, and to the anastomosis between nerve fibres observed along the edge of the rectal sheath. In some cases pain is so severe that it has been felt on the opposite side but in a milder form.

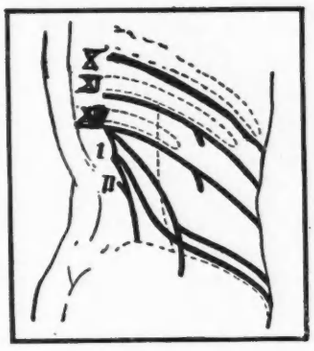


Fig. 1

The following table head shows the approximate spinal segments to which pain is referred from the various viscera.

Intestine	9th to 12th dorsal
Gall bladder	Mostly 9th dorsal
Kidney	Mostly 10th dorsal, also 11th and 12th dorsal and 1st lumbar
Ureter	11th and 12th dorsal, 1st lumbar
Testis	10th dorsal
Epididymis	11th and 12th dorsal
Ovary	10th dorsal
Fallopian tubes	11th and 12th dorsal
Bladder	11th and 12th dorsal and 1st lumbar, also 3rd and 4th sacral
Uterine cervix	11th and 12th dorsal and 1st to 4th sacral
Uterine body	10th dorsal to 1st lumbar

It is noted here that the 10th dorsal segment carries most of the renal stimuli, but according to Levitas the 12th dorsal and 1st lumbar segments receive most of the stimuli from the renal pelvis and the ureter. The skin around the umbilicus is supplied by the 10th dorsal and below this by the 11th and 12th dorsal. The skin over the pubes, scrotum and inguinal region is supplied by the ilio-hypogastric and ilio-inguinal comprising the 1st lumbar.

The initiation of the painful stimuli is carried by the autonomic nervous system from the renal pelvis and ureter to those parts of the abdominal wall supplied from the 10th dorsal to the 1st lumbar. Levitas has mapped out diagrammatically 5 points of tenderness (Fig. 2).

1. Below the 12th rib lateral to the spines of the 1st lumbar vertebræ.
2. The posterior curve of the crest of the ilium.
3. The maximum area of tenderness which is a spot about the size of a half dollar one inch in front of the anterior superior iliac spine and on the same level. Just here the 12th dorsal and 1st lumbar emerge from the internal oblique muscle.
4. Just above and lateral to the pubic crest.
5. Along the femoral canal in Scarpa's triangle. (The femoral branch of the genito-femoral 1-2L.)

Muscle spasm is more often found in the external oblique than the rectus abdominis.

Randall and Hughes have divided these stimuli into intrinsic and extrinsic, the former arise from negative nerve endings within the urinary tract whereas the latter arise from spinal nerve endings in the peri-renal and peri-ureteral parietal peritoneum. The intrinsic stimuli pass from peri-renal and peri-ureteral inflammation from direct contact with the outer surface of the parietal peritoneum and gives fairly definite localization in one of the four quadrants of the body.

It is a well known fact that individuals vary in their sensitivity to pain. A small calculus may be passed by one person without the necessity of a hypodermic, whereas in another the passage of a similar calculus may require several hypodermics.

Almost all lesions of the urinary tract (renal and ureteral calculi, hydronephrosis, ureteral stricture, tumour, polycystic kidneys, nephroptosis, etc.) may mimic intra-peritoneal disease. In some the acute abdominal symptoms may overshadow those confined to the kidneys and to

* Read at the Seventy-first Annual Meeting of the Canadian Medical Association, Section of Urology, Toronto, June 20, 1940.

add to the confusion the urinary signs may be minimal or absent. The number of cases which have had abdominal operations for urological conditions are legion. Our old friend the appendix has been removed innumerable times when the trouble has really been in the kidney or ureter. The differential diagnosis between acute pyelitis and acute appendicitis in children is often difficult. The temperature in acute pyelitis is usually higher and it is a good working rule that in acute appendicitis the temperature rarely goes over 103° although I have seen one or two cases where it has. The pain in acute appendicitis usually starts over the solar plexus and later shifts to McBurney's point; in pyelitis the pain should be found in the back and down the ureter. In a small child this history may not be clear. Moreover, the appendix may be lying close to the ureter and consequently some blood and pus cells may be found in the urine. In the beginning of pyelitis very little pus may be found in the urine; moreover, in some cases of pyelitis the tenderness seems to be more marked over the ureter than in the kidney region. The rigidity of a very acute appendicitis is not seen in pyelitis, but resistance in the external oblique may be present. Chills are frequent in pyelitis but I have seen them in one or two cases of acute appendicitis and it means a tense gangrenous appendix on the point of rupturing. Vomiting may be present in both conditions.

Typical white blood counts of lesions which may enter into the differential diagnosis are as follows:

1. *Influenza.*—There is no leucocytosis but there may be a relative increase in lymphocytes.
2. *Appendicitis.*—There is a leucocytosis of from 8,000 to 20,000 with a relative increase of polymorphonuclears to 80 or 92 per cent, both depending on the acuteness of the condition. When an appendiceal abscess develops, the count remains high but if the pressure lessens and it begins to absorb there is a fall in the count and a relative increase in the lymphocytes.
3. *Pneumonia.*—Here the total count is high—20,000 to 30,000 with a relative increase of polymorphonuclears up to 95 per cent.
4. *Pyelitis.*—There is no clear cut picture. When the infection is due to *B. coli*, which is the most frequent organism found, there is no leucocytosis or if any it is very slight. If the organism is staphylococcus or streptococcus there will be some leucocytosis. The acuteness of the condition will also affect this or more important still, if there is any blockage in the drainage from the pelvis.
5. In peri-nephritis or sub-phrenic abscess the white blood count is always high in the neighbourhood of 20,000 and with a relative increase in polymorphonuclears around 90 per cent.

The commoner urological lesions liable to be confused with the sub-acute or chronic appendix are renal and uretic calculi hydronephrosis, tuberculous kidney, kinks and strictures of the ureter, etc.—calculus, of course, being the most frequent offender. The pain of renal calculus becomes more severe almost at once and is fairly continuous. That of appendicitis is of gradual onset and often intermittent due to peristalsis. Renal colic may be unbearable and the patient found rolling on the floor—the pain may be referred to the genitals —there may be frequency and the urine may be red with blood. Others may have only occasional red blood cells on microscopic urinalysis, and the pain localized and not referred.

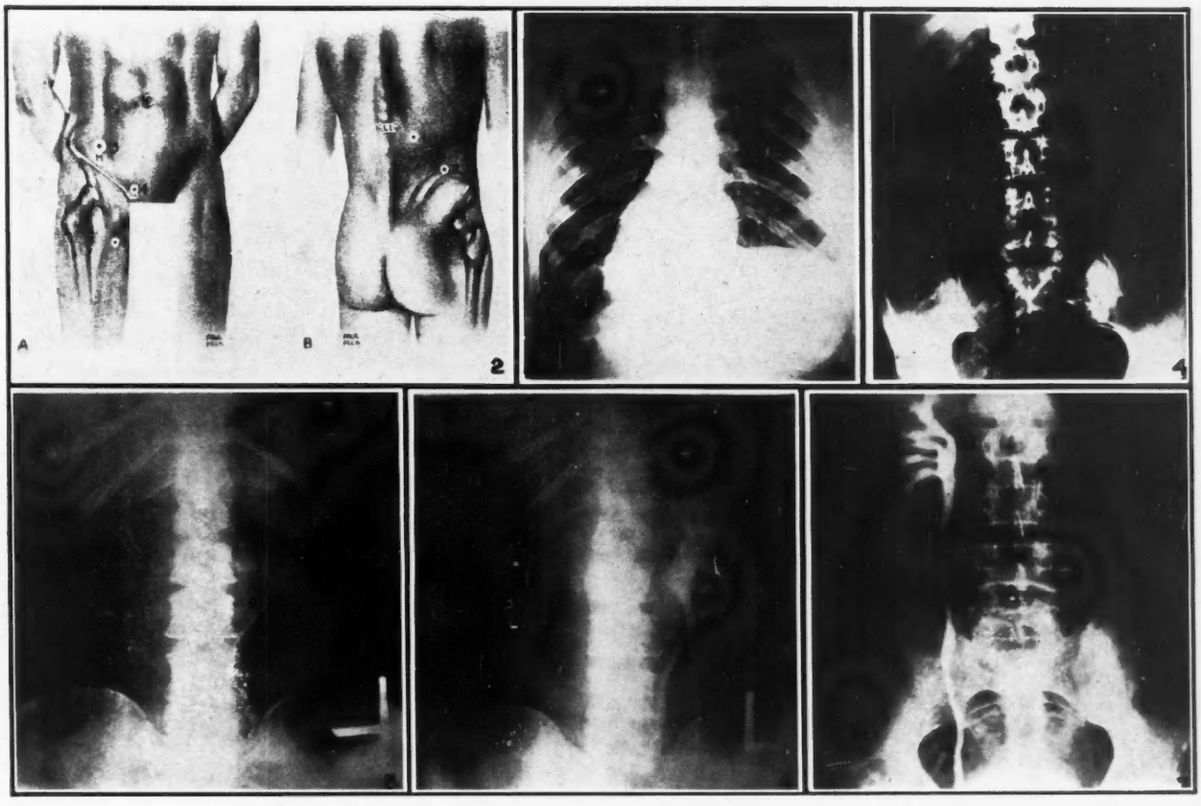
In colic, pain and tenderness disappear almost simultaneously, whereas, in appendicitis tenderness may be present for some days after the pain has gone. The moral here is to take time and investigate such cases thoroughly, by a careful physical examination, microscopic urinalysis, x-rays, etc. This was brought home to me rather forcibly some years ago. We were changing our x-ray outfit in our office, and the salesman who had been casting glances at our stenographer suggested trying the machine out on her when he got it set up. An x-ray was taken of her spine. Imagine our amazement when a fairly large stone showed up in the right kidney. We had taken her appendix out a short time previously.

Lesions of the gall bladder may be confused with urological conditions. In some cases renal pain is referred into the right upper quadrant through the 9th and 10th cord segments and thus over ride the area of the gall bladder pain. The shadow of the cholecystogram may lie directly over a renal calculus, and if care is not taken mistakes will occur. I would like to cite an illustrating case.

Mrs. J.E.F., aged 44, admitted to Royal Inland Hospital, Kamloops, 1937. Previously had suffered severe attacks of colic in the right upper quadrant. Tenderness more marked over the gall bladder than over the kidney area. Cholecystogram showed what appeared to be a gall stone. For many years had had recurrent attacks of right sided pyelitis and pus and *B. coli* frequently found in the urine. A cholecystectomy was decided on but when the abdomen was opened the gall bladder was found to be normal. A long needle discovered the calculus in the pelvis of the right kidney. The peritoneum was closed and then reflected inwards and the stone removed by the anterior route. She made an uneventful recovery.

Very rarely kidney and gall stones co-exist and these make a nice problem in differentiation close studies of both organs with regard to function tests as well will be necessary.

Subphrenic abscess, perinephritic abscess, and *acute pyelitis* are conditions which have to be differentiated in certain cases. Pain and tenderness in the kidney area with fever and chills may be present in all three. In acute pyelitis pain and tenderness are found in the kidney area and down the ureter and into the bladder with fever and frequency. Pus and bacteria are found in the urine although these may be scanty until after 24 hours or so. Points of difference, however, arise in the history and examination which help materially in the diagnosis.



Subphrenic abscess usually follows a perforated peptic ulcer—one which has a small leak and where the fluid has collected around the liver. It can also be a complication of acute cholecystitis or follow after a retro-cæcal appendicitis where the pus has worked upward. The kidney in such cases is displaced downwards and the diaphragm on that side elevated and a fluid level may be seen with gas in the x-ray. Urinalysis is negative.

CASE HISTORY

W.F., male, aged 20, admitted to hospital July 5, 1938. One month previous had sore throat and this was followed by pain in the right side. There was a history of vomiting, later there was pain in the back and fever. Details were hard to get as he reported several weeks after the beginning of his illness. He looked haggard and septic although a big husky fellow. On examination there was tenderness in the right loin and around the flank into the right lower quadrant. This seemed to be the area in which the pain first started, that is, around the cæcum. There was marked tenderness in the area of the 12th rib. Urinalysis was negative; blood culture negative; white blood cells 25,000, polymorphonuclears 90 per cent; endophiles 9 per cent; eosinophiles 1 per cent. X-ray showed diaphragm raised on the right side. At operation, aspiration of pus found above and below the 12th rib. This was resected and good drainage provided, resulting in quick recovery. September 6, 1938—readmitted to hospital complaining of pain and discomfort around the cæcum. Appendix was removed and this was found retro-cæcal and sub-acutely inflamed, and in our opinion was the cause of the subphrenic abscess. (Fig. 3.)

Perinephritic abscess is formed in the perirenal fat outside the kidney and is blood-borne, usually from carbuncles. There is a bulging in the loin when the abscess is fully developed. The position of the kidney is normal and urinalysis is negative. X-ray shows obliteration of the psoas muscle shadow.

P.L.R., female, aged 20, admitted to hospital, September 19, 1939. History of recurrent boils and carbuncles for over a month. September 15th, developed a pain in the upper right quadrant and had a couple of chills. On admission September 19th, marked tenderness in region of kidney and hyperæsthetic area, downwards into the lower right quadrant. White blood cells 12,000 with rapid sedimentation rate. The differential diagnosis was (1) acute appendicitis, (2) acute pyelitis, (3) perinephritis abscess. The absence of rigidity and increased sedimentation rate and marked tenderness in costo-vertebræ angle pointed toward the kidney. Some pus was found in the urine. Some days later fullness developed in the costo-vertebral angle, and pus disappeared from the urine. A flat x-ray plate showed ob-

literation of the psoas muscle shadow. October 2, 1939, an incision was made over the most prominent area, the abscess opened, and well drained. An uneventful recovery followed (see Fig. 4).

Hydronephrosis or large cysts of the kidney may give great difficulty in diagnosis since they may develop without pain and may be first seen in their later stages with a tumour filling most of the abdomen. They will have to be differentiated from the various ovarian cysts, pancreatic cysts and hydatid cysts. Dullness in the flanks is a constant sign in cysts or hydronephrosis of the kidney. Pyelograms will show if a hydronephrosis is present or if not, the position and shape of the pelvis can be seen. Tumours elsewhere may displace the pelvis or as in the following case a large cyst of the kidney pushed the pelvis beyond the spinal column to the opposite side.

Mrs. D., aged 52, referred by Dr. Beech of Salmon Arm, July 11, 1937. For a period of 10 years had noticed a swelling gradually developing in the right side of the abdomen, which filled and distended the right side. It was impossible to get one's fingers between the mass and the costal cartilages. Dullness extended from the spine on the right side close to the midline in front. Plain x-ray showed no gas or bowel loops on the right side. Gall bladder dye x-ray gave no shadow. Cystoscopic examination showed a normal bladder. Both ureters easily catheterized. The pyelogram was difficult to read but it showed what we thought was a double kidney or the pelvis of the right kidney pushed over past the mid-line until it was superimposed over the left and almost beyond it.

An operation July 16, 1937—a long incision lateral to the right rectus was made; on opening the abdomen a retro-peritoneal cyst was seen; this proved to be a large solitary cyst of the kidney and it was removed intact with the kidney, weight being 7½ pounds. (Figs. 5 and 6.)

Occasionally malignant or inflammatory lesions exist outside the bladder which by their proximity may cause urgent bladder symptoms and these may be the patient's only, or at any rate the chief complaints.

Carcinoma of the colon if contiguous to the bladder may invade it directly and give symptoms of acute cystitis. Carcinoma of the ovary may act in the same way or cause obstruction of the ureter from direct pressure, resulting in pain in the kidney and bladder region with resulting frequency.

Diverticulitis of the colon may result in abscess formation which may burrow close to the bladder or even rupture into it. Marked symptoms of pain and urgency result.

An illustrating case is the following:

J.P., aged 60, referred by Dr. Underhill of Kelowna. Patient, a rather emaciated individual complained chiefly of frequency and burning for several months past. There had been no appreciable change in the bowel movements. There had been considerable loss of weight. In the supra-pubic region there was a mass present a little to the left and it was extremely tender. The urine contained a great deal of pus and heavy bacteria. Kahn—negative; spinal fluid—negative; non-protein nitrogen, 50 mg. per 100 c.c. Cystoscopic examination showed a frayed ulcer above and internal to left ureteric orifice. Catheter passed easily to right kidney and pyelogram and urine from this kidney was normal. The left catheter passed up 2 inches or so and met an obstruction and the catheter could be seen most of this distance curling around some mass. The abdomen was opened and a large carcinoma found on the sigmoid attached to bladder. It was apparently on one side of the bowel and had produced very little obstruction. A colostomy was done but the patient died of emaciation, really worn out from his bladder condition. At autopsy one could pass a finger from the bowel into the bladder. This tumour had infiltrated into the bladder and the patient's most marked symptoms were all referred to the bladder. (Fig. 7.)

On the other hand, patients with chronic urinary retention may complain chiefly of upper abdominal distress with nausea and vomiting.

Endometriosis of the urinary bladder, a rare complication of this condition is characterized by cyclic attacks of frequency, dysuria and hæmaturia. Cystoscopic examination shows the black or blue domed cysts and generalized congestion. Artificial menopause is the treatment of choice.

There remains a large number of cases which have pain in the region of the kidney and for which, after careful examination, no definite cause can be found. The neurasthenic individual with enteroptosis and tender areas here and there all over the abdomen are more liable to have movable kidneys,—Dietl's crisis and spastic strictures of the ureters. Pain in the kidney region may not be due to any urological lesion but may be caused by arthritis or osteomyelitis of the spine, herpes of the 12th and 1st lumbar nerves, neuritis of unknown cause and myositis, etc. Probably many of these pains are similar to the pleurodynias found in the chest. If a tender area can be found at the edge of a spine where these nerves emerge, a good working rule is to put on a fly blister about 2 inches in diameter and see if this clears up the pain, which it probably will do for a time if it is an ordinary neuritis. Afterwards, one of the local anæsthetic solutions which have a prolonged action can be injected.

TECHNIQUE IN ESTABLISHING THE DIAGNOSIS OF GENITO-URINARY MALFORMATION*

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GENITO-URINARY malformations give rise to a number of conditions, for example, pyuria, hydronephrosis, hydroureter, enuresis, hypertension, uræmia, etc. The early establishment of a diagnosis of abnormality of the genito-urinary tract frequently lends itself to surgical correction of the malformation with relief of symptoms, whereas the delayed recognition often allows continuation of the deleterious effects which in the end so seriously damage the urinary function.

Much of the investigation for the diagnosis of many of the malformations seen can be carried out by the attending physician if he is familiar with the technique. The procedures used in the pædiatric department of the Hospital for Sick Children will be described.

History-taking and clinical findings.—A careful, complete history and physical examination are most essential; for example, if the child is male, has always had enuresis with a small stream, and on examination presents an enlarged bladder, a diagnosis of urethral obstruction, probably congenital post-urethral valves, is almost certain.

Routine laboratory investigation.—The examination of the urine for sugar, albumin, microscopic, specific gravity, and reaction is essential. The finding of more than 4 pus cells per high-powered field of fresh uncentrifuged urine indicates a pathological condition. This constitutes a diagnosis of pyuria except when it is found in a dehydrated toxic patient. In a dehydrated patient the urine will be concentrated so much that it will show pus microscopically. Accordingly, in young dehydrated children it is necessary to obtain a second specimen containing pus after the child has received fluids, before definitely diagnosing pyelitis. The albumin test is usually positive. The reaction is frequently strongly acid in infections of the upper urinary tract and alkaline when in the bladder. Constant low specific gravity suggests a loss of kidney function or diabetes insipidus. When pus is discovered bacteriological cultures are made on urine obtained by catheter.

Kidney function tests.—Non-protein nitrogen and creatinine of the blood are estimated, to determine the retention of nitrogen products caused by decreased function of the kidney. Also this is necessary before intravenous and retrograde pyelography because if the function of the kidney is markedly decreased these procedures are dangerous. The intravenous method of pyelography depends on kidney excretion, and if this function is low the value of the test is decreased. Other kidney function tests, such as concentration, two-hour test, dye excretion, and urea clearance, may be carried out if indicated.

X-ray investigation.—A flat plate of the abdomen, to cover the kidney, ureters and bladder, is taken chiefly to reveal stones in the urinary tract. However, it may also reveal abnormalities of the spine, such as spina bifida occulta, which may be associated with neuromuscular dysfunction of the urinary tract.

The next step taken is the cystogram. This is a relatively simple procedure, and when abnormalities are demonstrated by this method it is done very definitely. However, it must be clearly understood that lack of abnormal findings by this method does not preclude the possibility of abnormality of the genito-urinary tract.

The method is to catheterize the patient and leave the catheter in the bladder. It is usually fastened in place with adhesive. Twelve and one-half per cent sodium iodide solution is injected into the bladder until the child signifies either verbally or by facial expression that voiding is imminent. An x-ray in the antero-posterior direction is taken and also a lateral with the catheter in place, then a second antero-posterior with the catheter removed. By this method one outlines the bladder which normally is quite smooth and round. If the outline is irregular it indicates inflammation, diverticulation, or

* From the Department of Pædiatrics, University of Toronto, and the Hospital for Sick children, under the direction of Alan Brown, M.D., F.R.C.P.(Lond.).

Read at the Seventy-first Annual Meeting of the Canadian Medical Association, Section of Pædiatrics, Toronto, June 19, 1940.

trabeculation of the bladder. Normally there is no reflux up the ureters; if this occurs it indicates a loss of uretero-vesical valve function which most frequently is a result of local infection, neuro-muscular dysfunction, back pressure from obstruction lower down, and congenital elongation and kinking of the ureter. Obstruction in the urethra shows the outline of the base of the bladder to be funnel-shaped instead of the usual flat contour.

Intravenous pyelography has recently become popular owing to the discovery of radio-opaque solutions which are excreted by the kidney in sufficient concentrations to allow the upper urinary tract to be outlined in this manner. Diodrast is the solution employed by us, and 20 c.c. are injected intravenously with infants and children. The preparation of the patient is most important to obtain satisfactory results. The chief difficulties are: (*a*) gas in the bowel obscuring the excreted material; (*b*) insufficient concentration of the excreted material to obtain a satisfactory picture; (*c*) too rapid passage of the material from the kidney pelvis to the bladder, so that the pelvis and calyces are not outlined.

To increase the concentration of the dye no fluid is allowed for 12 hours prior to the test. For purposes of removing gas and interference by bowel content, cascara is given the previous

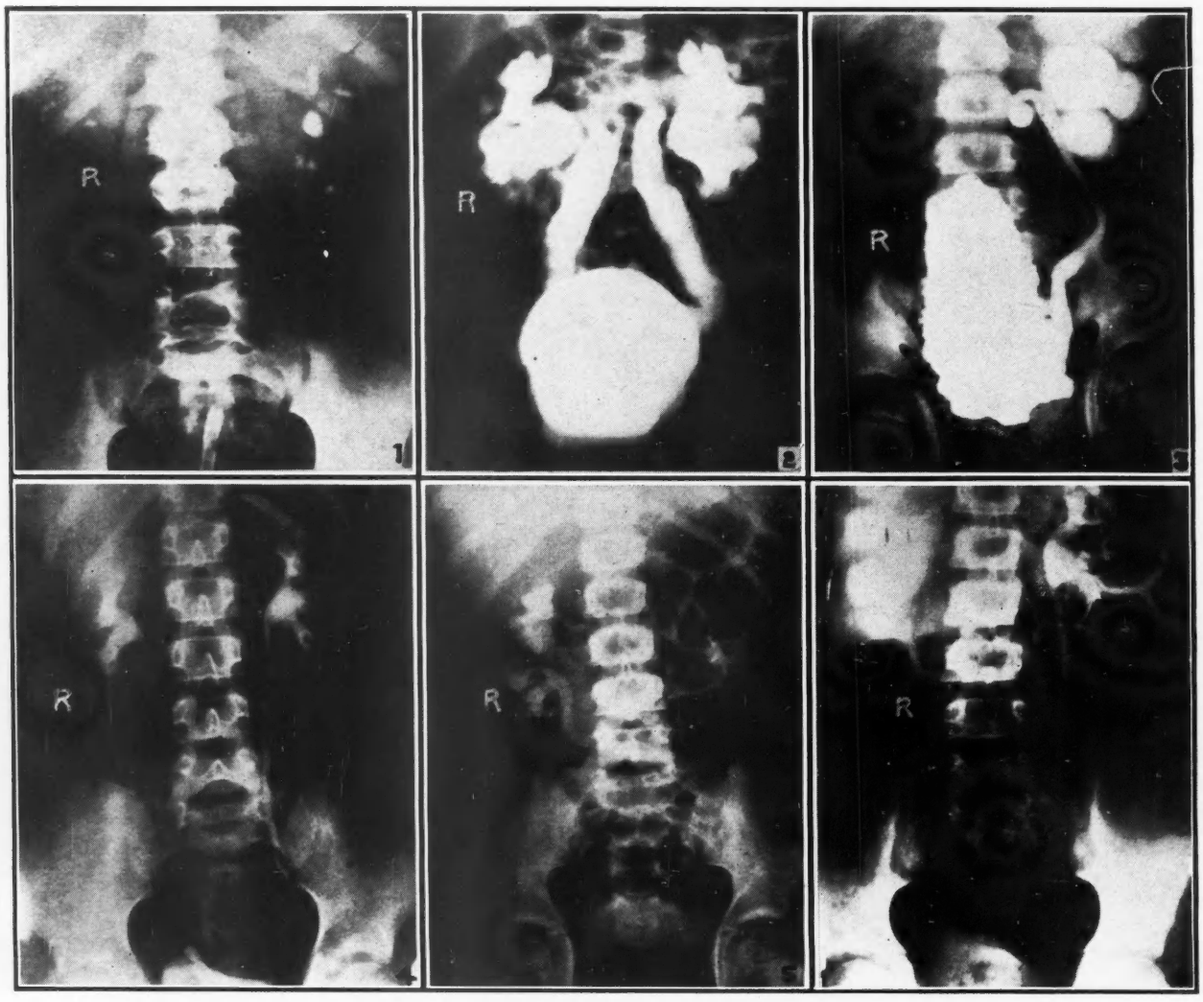

Fig. 1—Flat plate of abdomen (K.U.B.) showing stones in pelves and calyces of both kidneys. Diagnosis, renal calculi. **Fig. 2.**—Cystogram on an 8 months old female with persistent pyuria, showing reflux with dilatation of both ureters and hydronephrosis. Diagnosis, hydronephrosis and hydroureter due to neuro-muscular dysfunction. **Fig. 3.**—Cystogram on an 11-year old boy with persistent enuresis and dribbling. Bladder shows distension and irregular outline with marked trabeculation. The important finding is the triangular prolongation of the bladder outline down into the urethra, proving the diagnosis of posterior urethral valves. There is an associated hydronephrosis. **Fig. 4.**—Normal intravenous pyelogram. **Fig. 5.**—Intravenous pyelogram showing bilateral reduplication of ureters and pleves of both kidneys with slight hydronephrosis on the right. The patient was a 5-year old female with persistent pyuria. **Fig. 6.**—Intravenous pyelogram on a 13-year old boy with persistent pyuria, showing unilateral hydronephrosis on the right side. Further investigation revealed an aberrant vessel at the lower pole of the right kidney.

night; a 1.2.3. enema is given one hour before the test, followed in half an hour by 0.5 c.c. of pitressin or 1 c.c. of prostigmin, a rectal tube is inserted and it is important that this be placed as high as possible. To keep the dye in the upper urinary tract and also to press any remaining gas out of the field of observation, pressure is maintained over the bladder by means of a cotton ball fastened down with canvas retaining strap attached to the sides of the x-ray table or the special frame which has been devised in the Hospital for Sick Children. As much pressure as the child will tolerate is advisable, as this makes for better retention of the dye in the upper urinary tract and better outlining of the pelves and calyces of the kidney.

The injection of the 20 c.c. of diodrast is given slowly into a vein after the patient is on the x-ray table or frame with the pressure applied. Much discomfort and reaction are avoided if the diodrast is warmed. X-rays are taken antero-posteriorly of the whole genito-urinary tract at 3 minutes, 5 minutes, 10 minutes, and 15 minutes after the administration of the diodrast is completed. These x-rays, if satisfactory, will outline the pelves, calyces and ureters of both kidneys. In the event of one side not being outlined the test should be repeated in 24 hours, and if the result is duplicated it indicates the presence of an abnormality. By this method one may find evidence of hydronephrosis due to various causes, kinking and obstruction of the ureters, congenital abnormalities of the kidneys, etc.

Cystoscopy and retrograde pyelography are surgical procedures, and are the final and most thorough method of investigation. They are used to confirm and amplify abnormal findings discovered by the other methods and to make diagnosis where satisfactory results cannot be obtained by the less drastic procedures.

SUMMARY

When a patient is seen in whom a genito-urinary abnormality is suspected the following investigation should be carried out: (*a*) a complete history and physical examination; (*b*) repeated urinalyses, particularly microscopic examination of the fresh uncentrifuged specimen. If the findings from these tests indicate any possibility of abnormality then special laboratory procedures such as for blood non-protein nitrogen, creatinine, and kidney function tests should be done. Following that, x-ray examinations, such as the flat plate of the abdomen, the cystogram, and the intravenous pyelogram should be done. Cystoscopy and retrograde pyelography are used to confirm and amplify the findings to the other methods.

TREATMENT OF PNEUMONIA IN CHILDHOOD*

BY R. R. STRUTHERS

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SINCE the introduction of chemotherapy in the treatment of pyogenic infection in human beings there has been widespread application of the use of sulfanilamide and sulfapyridine in the treatment of streptococcal and pneumococcal infections. During the past two years the treatment of pneumococcal infections by sulfapyridine has become a routine procedure on this continent. The object of the present communication is to review the results of the treatment of pneumonia in infants and children by this drug. To this end, the case records of children suffering from pneumonia, either of lobar or bronchial distribution, admitted to and so treated in the Children's Memorial Hospital, Montreal, between October 1, 1938, and March 31, 1940, a period of eighteen months, have been reviewed; from this review certain conclusions may be drawn. No attempt has been made in this study to review the very extensive literature on the treatment of pneumococcal pneumonia in children, which has rapidly accumulated.

The present study concerns the case reports of 219 patients, 203 of which are sufficiently complete to permit of their inclusion here. In making the differential diagnosis between lobar and broncho-pneumonia the history, clinical signs, and x-ray examination of the flat plate of the chest were correlated, as regards the distribution of the pneumonic lesion and its lobar

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or bronchial character. Typing of the infecting organisms was carried out in comparatively few cases; of those that were typed, Type 3 appeared four times, Type 6 three times and Type 14 three times, the remainder being distributed over Types 1, 2, 5, 7, 18, 19, 23 and 27. The sparseness of the reports of typing precludes any conclusions.

Of these 203 patients 105 were males and 98 females, the average age of the males being 2 years 9 months and the average age of the females 4 years 5 months. There were 87 cases of broncho-pneumonia, of which 46 were males and 41 females, and 116 cases of lobar pneumonia, of which 59 were males and 57 females (Table I). Referring to Table II, it will be

TABLE I.
USE OF SULFAPYRIDINE IN PNEUMONIA

Broncho:	Males.... 46	87	203	105—Males	
	Females.. 41				
Lobar:	Males.... 59	116		98 Females	
	Females.. 57				

Ages:	Average age of males....	2 years 9 months
	Average age of females...	4 years 5 months
Broncho:	Average age.....	1 year 9 months
	Males....	1 year 6 months
	Females..	2 years 6 months
Lobar:	Average age.....	4 years 6 weeks
	Males....	2 years 1 month
	Females..	6 years 2 weeks

Mortality:		
	Broncho-pneumonia.....	4
	Lobar pneumonia.....	1
		5

TABLE II.
USE OF SULFAPYRIDINE IN PNEUMONIA
From October 1, 1938 to March 31, 1940

Month	*Broncho*	*Lobar*	*Total*
January.....	4	6	10
February.....	11	10	21
March.....	26	19	45
April.....	14	12	26
May.....	8	11	19
June.....	5	13	18
July.....	5	1	6
August.....	2	2	4
September....	1	5	6
October.....	4	7	11
November....	4	18	22
December....	4	10	14 = 203

noted that the frequency of pneumonia increases during the winter and spring months; the frequency of lobar pneumonia rises during the fall and early winter, and that in the late winter, associated with the frequency of those infectious diseases of which broncho-pneumonia is recognized as being a common complication, this type of pneumonia is much more marked.

The average dose of sulfapyridine in all cases was 1.39 grains per pound, and the average total dose given was 158.74 gr. Of 74 cases which showed some toxic effect from the drug the average dose per pound producing toxic effects was 1.09 gr., whereas the average dose in those patients who showed no toxic effect from the drug was 0.88 gr. per pound. It is to be noted that there is a difference of approximately 20 per cent in these two groups, suggesting that equally good results can be produced without the administration of doses sufficiently large to produce evidence of toxic effect, and that from three-quarters to four-fifths of a grain per pound will produce the desired curative effect without evidence of toxicity (Table III).

The drug was administered either in tablet form to the older children or in an emulsion to infants, given by mouth, and produced varying toxic effects, these being principally vomiting and/or diarrhœa, cyanosis, skin rashes, leukopenia, severe anæmia, or hæmaturia. In certain

TABLE III
USE OF SULFAPYRIDINE IN PNEUMONIA

Average dosages		
Average total dose of all cases.....		158.74 gr.
Average dose of all cases per lb.....		1.39 gr.
Average total dose producing toxic effects....		129.32 gr.
Average dose producing toxic effects per lb...		1.09 gr.
Average total dose producing no toxic effects.		177.54 gr.
Average dose producing no toxic effects per lb.		0.88 gr.
Average total dose in complicated cases.....		167.54 gr.
Average dose in complicated cases per lb.....		1.05 gr.
Average dosage: Broncho—Total.....		135.67 gr.
Gr. per lb.....		1.77 gr.
Lobar —Total.....		181.81 gr.
Gr. per lb.....		1.02 gr.

severely ill children the drug was administered by intravenous route in the form of sodium sulfapyridine or "soludagenan" (Poulenc Frères, Montreal). The method of intravenous administration of sodium sulfapyridine which we have used is based on the same principles as the oral administration of sulfapyridine. The drug is prepared in 3 c.c. ampoules containing 15 grains (1.0 g.) of sodium sulfapyridine. It is easily miscible with normal saline and is administered by intravenous drip. The dosage is calculated according to the weight and age of the patient. It has been our experience that 1 gr. per pound of body weight is adequate in most cases to obtain a satisfactory concentration in the blood. However, in some instances as much as 1½ gr. per pound of body weight has been tolerated

for as long as 48 hours. This is particularly true in children under two years of age. Sixty gr. a day is considered a maximum dose. For example, a child weighing 45 pounds would receive 1 ampoule (15 grains) in 200 c.c. of normal saline every 8 hours for 24 hours, making a total of 45 gr. If it is administered slowly no difficulty should be encountered. In infants it is the usual practice to give intravenous medication by means of "cutting down", usually on the great saphenous vein at the level of the internal malleolus. The needle has often been left in place as long as 72 hours without any untoward results. In older children the intravenous fluid medication is usually administered through one of the veins in the ante-cubital space. When there is no evidence of dehydration sodium sulfapyridine may be administered by the intramuscular route. One ampoule of the drug is diluted to 20 c.c. with sterile water, making a dilution of 15 grains in 20 c.c. All, or part of this, is then injected into one or both buttocks every 6 hours according to the prescribed total dosage.

TABLE IV.
USE OF SULFAPYRIDINE IN PNEUMONIA

		BLOOD CONCENTRATIONS IN 25 CASES	
No.	*Day of disease*	*Days after starting drug before temperature normal*	*Blood level after 48 hours Percentage*
			mg.
1	Third	Third	5.59
2	Ninth	First	6.40
3	Seventh	Second	6.49
4	Third	Second	7.25
5	Fourth	Second	5.19
6	Third	Second	7.42
7	Fifth	Second	6.74
8	Fourteenth	Second	6.40
9	Sixth	Second	8.29
10	Third	Second	8.52
11	Fifth	Second	8.62
12	First	Second	2.62
13	Third	Third	6.29
14	Sixth	Third	5.46
15	Fifth	Second	5.80
16	Fifth	Second	6.43
17	Third	Second	2.42
18	Second	Second	10.70
19	Fourth	Third	6.69
20	Seventh	Second	9.78
21	Second	Second	2.40
22	Seventh	Second	6.58
23	Second	Second	7.83
24	Third	Second	1.02
25	Fourth	Third	4.80

Table IV shows the blood levels of sulfapyridine of 25 patients suffering from pneumonia, who had been given 1 gr. per pound of the drug by mouth. The average blood level after 48 hours' administration of the drug was 6.3 mg. per cent. Long[1] has suggested that a blood level of 4 mg. per cent is a more or less critical level for the successful treatment of pneumonia during the early stages of the disease. As the levels produced in children of this group were considerably higher than this it is again suggested that a dose of less than 1 grain per pound is adequate for the production of a satisfactory blood level (Table IV). It has not been routine to administer sodium bicarbonate with sulfapyridine, excepting in those cases which showed hæmaturia. In the presence of hæmaturia an attempt was made to produce rapid alkalization of the urine, with the object of redissolving the crystals of sulfapyridine and eliminating the drug from the genito-urinary tract.

The study of 203 cases showed that the average duration of fever before chemotherapy was instituted was 136 hours, and the average duration of fever after therapy 39 hours, with a maximum of 25 days and a minimum of 8 hours (2 doses). To those of us who have been previously accustomed to seeing a child with lobar pneumonia suffer from pyrexia and breathlessness and the other distressing evidences of pneumonia for a period of five to seven days the evidence of signs of convalescence after 12 to 24 hours of sulfapyridine therapy is little other than miraculous. In many cases the effect of the administration of the drug is as striking as the effect of the administration of specific serum, previously seen in the treatment of pneumonia in adults. Scott[2] has already reported that the febrile course of treated patients in his series averaged 4.94 days, and that the febrile course of the control group averaged 7.39 days.

Evidence of toxæmia tended to disappear *pari passu* with the fall in temperature, which on the average reached normal in 39 hours after the beginning of treatment. Rarely did evidence of toxicity continue more than twelve hours after the temperature reached normal level. Occasionally secondary rises in temperature occurred before the treatment was discontinued. Following the cessation of therapy the temperature, in the absence of complications, remained normal. In the 203 cases there were 5 deaths, four in the group suffering from broncho-pneumonia, and one child, aged 4 weeks, who died from a pulmonary abscess secondary to lobar pneumonia.

The complications may be divided into two groups, those which may be regarded as complications of the infection, and those which may

be considered evidences of toxicity from the administration of sulfapyridine. As complications of the disease, otitis media appeared in 42 cases, mastoiditis in 5 cases, lung abscess in 1 case, sinusitis in 2 cases, and 1 case of empyema, from which sterile pus was aspirated and which resolved spontaneously (Table V).

TABLE V.
USE OF SULFAPYRIDINE IN PNEUMONIA

COMPLICATIONS OF THE DISEASE	
Otitis media	42
Mastoiditis	5
Empyema	1
Lung abscess	1
Sinusitis	2

Toxic effects of the drug were noted in 74 cases. Vomiting and/or diarrhœa occurred 30 times in the broncho-pneumonic group and 20 times in the lobar pneumonic group. One patient in each of these two groups died. Cyanosis, of a degree to be commented upon in the case report, occurred four times in the broncho-pneumonic group and five times in the lobar pneumonic group; hæmaturia, which, as well as skin rashes, was considered an indication for the immediate cessation of treatment, occurred once in the broncho-pneumonic group and 5 times in the lobar-pneumonic group. With reference to the cases showing hæmaturia it is to be noted that the average total dose of all cases was 158.74 gr., whereas in the patients showing hæmaturia the average total dose was 397.16 gr., which would suggest that hæmaturia is produced as the result of more or less long continued administration of the drug, even though the average dose per pound of the group was only 0.96 gr. We are unable to show any definite relationship between the onset of the toxic effects of the drug and the blood level of sulfapyridine. Sixteen cases of leukopenia were encountered; where there was a fall of the total leucocyte count below 8,000 and a granulocytic percentage below 30, it was considered an indication for the cessation of the administration of the drug. Severe degrees of leukopenia were not encountered. Severe anæmia which could be considered a result of the administration of sulfapyridine occurred in only one case, following a total dosage of 757 gr. Treatment was discontinued because of toxic effects of the drug in only twelve cases (Table VI).

TABLE VI.
USE OF SULFAPYRIDINE IN PNEUMONIA

AVERAGE DURATION OF FEVER		
Average duration of fever before therapy		136 hours
Average duration of fever after therapy		39 "
	Maximum	25 days
	Minimum	8 hours
Average duration of fever after therapy in		
Broncho-pneumonia		39 hours
Lobar pneumonia		37 hours

Toxic effects	*Broncho*	*Lobar*	*Total average dosage grains*
Vomiting and/or Diarrhœa	30	20	102.45
Cyanosis	4	5	147.00
Skin manifestations	4	1	112.00
Hæmaturia	1	5	397.16
Hæmolysis (severe anæmia)		1	757.00
Leukopenia	16 cases		134.00

Therapy discontinued because of toxicity in 12 cases.

TABLE VII.
USE OF SULFAPYRIDINE IN PNEUMONIA

SUMMARY	
A REVIEW OF 203 CASES OF LOBAR AND BRONCHO-PNEUMONIA	
Average duration of fever before therapy	136 hours
Average duration of fever after therapy	39 hours
Toxic effects produced in 74 cases— Average dose per lb	1.09 gr.
No toxic effects produced in 129 cases— Average dose per lb	0.88 gr.
Cessation of treatment indicated by: Hæmaturia Leukopenia Skin rash Vomiting and/or Diarrhœa.	

SUMMARY

From a review of 203 cases of pneumonia treated with sulfapyridine in a children's hospital it was found that the average duration of fever before treatment was 136 hours, and the duration of fever after therapy was begun was 39 hours.

Evidences of toxicity of the drug occurred in 74 cases; such toxic reactions were encountered when the average dose per pound was 1.09 gr. No toxic effects were observed when the average dose was 0.88 gr. per pound. This would suggest that a dose of somewhat less than 1 gr. per pound is sufficient to produce the desired result without danger of toxic manifestations. However, in those patients who showed evidences of toxicity from the drug this was produced by an average total dose of 129.32 gr., whereas the average dose of the whole group was 158.74 gr. From this it would appear that

the frequency of evidences of toxicity from the drug is a factor probably only of the dose per pound per day and not of the total administration of the drug in that the administration was usually arrested when toxic signs appeared. The average dose per pound of the whole group was 1.39 gr.

The mortality rate for the whole group was 2.5 per cent (4.5 per cent in the broncho-pneumonic group and 0.86 per cent in the lobar pneumonia group).

Complications of the disease occurred in 32 per cent and evidence of toxicity of the drug in 36.4 per cent. It would appear that an average dose of 1 gr. per pound is effective for the cure of the disease and the production of sulfapyridine blood levels of 6 mg. per cent or more, but that evidences of toxicity from the drug occur more frequently when the dose is greater than 9/10 of a gr. per pound, and we would suggest that an average dose of ¾ gr. per pound per day is likely to be quite adequate for therapeutic effect and less likely to produce toxic effects. It is to be noted that only one case of empyema was encountered in this group. The average stay in hospital for cases treated in this group was 19 days. It is our belief that the indications for the cessation of sulfapyridine are hæmaturia, leukopenia, skin rashes, and vomiting and/or diarrhœa. Examination of the urine at least every two days for evidence of hæmaturia or sulfapyridine crystals should be a routine procedure during the administration of the drug, and if such evidence be found fluids should be forced and a sufficient quantity of sodium bicarbonate administered to render the urine alkaline within 12 hours. Such measures have been found to be adequate for the relief of this complication. Other toxic manifestations subside promptly on the withdrawal of the sulfapyridine.

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RÉSUMÉ

Deux cents trois cas traités par la sulfapyridine entre octobre 1938 et mars 1940 font l'objet de cette étude. Chez 87 il s'agissait de broncho-pneumonie, et chez 116 de pneumonie lobaire. La durée moyenne de l'hyperthermie avant le traitement fut de 136 heures, et de 39 heures après le début du traitement.

On remarqua des signes de toxicité dans 74 cas; on remarqua, en outre, que ces signes apparaissaient lorsque la dose moyenne était de 1.09 gr. par livre de poids. Il semble démontré qu'une dose ne dépassant pas 1 gr. par livre de poids met nettement à l'abri des réactions toxiques. Il faut surveiller bien plus la dose totale par jour que la dose totale du traitement complet puisqu'il est toujours loisible de cesser dès le début des signes de toxicité.

Le taux général de mortalité fut de 2.5 pour cent. Des complications sont apparues dans 32 pro cent des cas et des signes d'intolérance au médicament ont été notés chez 36.4 pour cent des malades. Un pourcentage de 6 mg. de sulfapyridine dans le sérum sanguin paraît réaliser les conditions idéales. La dose de ¾ gr. par livre de poids et par jour met à l'abri de tout danger. Les indications de cesser la sulfapyridine sont l'hématurie, la leucopénie, les éruptions cutanées, les vomissements et la diarrhée. L'analyse des urines pour la recherche des cristaux de sulfapyridine doit être faite tous les deux jours, et dans les cas où ceux-ci sont présents, il faut augmenter la fréquence et la quantité des ingestions de liquides, et ajouter à la médication, du bicarbonate de soude en quantité suffisante pour alcaliniser l'urine dans les 12 heures. Les autres signes de toxicité disparaissent avec la cessation du médicament. J. SAUCIER

A FEW COMMON PROBLEMS IN INFANCY*

BY P. E. WILLIAMS

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Asphyxia neonatorum. — Although the death rate for the whole of infancy has been greatly reduced there has been slight if any decrease in the rate for the early hours and days of life. Asphyxia neonatorum takes its toll of these early deaths, and for this reason increased attention has been turned to this condition recently.

With the physician on the alert, evidences of beginning asphyxia may be detected before the baby is born. The following are some of the important suggestive signs: (1) violent fetal activity at or near term; (2) sudden excessive activity or convulsive movements during labour; (3) fetal bradycardia persisting between uterine contractions, irregularity of rhythm, weakness, and later tachycardia; (4) fetal heart rates above 160 and below 100 per minute.

Asphyxia neonatorum is divided into two types, asphyxia livida and asphyxia pallida. There are also intermediate forms, and one may pass into the other. Asphyxia livida is the common and less serious form. Cyanosis varies in extent and severity. The pulse is full and

* Read at the Seventy-first Annual Meeting of the Canadian Medical Association, Section of Pædiatrics, Toronto, June 20, 1940.

strong. Muscle tone is good. Respirations are absent or occur infrequently in short gasps. There is little difficulty in diagnosing this. Asphyxia pallida is the more serious type. The infant is severely shocked, atonic, and appears moribund. The skin is pale, and the mucous membranes are livid; the sphincters are relaxed and meconium oozes. The heart beat is weak, rapid at first, then slow. This form simulates severe brain injury so closely, and is associated with it so often, that there is practically no way to differentiate between them. Successful resuscitation leads one to the supposition that the condition was one of asphyxia.

Mild asphyxia livida usually responds readily to treatment. The more severe cases, particularly the prematures, require continued treatment to prevent repetition of the attacks or development of asphyxia pallida. The prognosis in the pallid form is poor, many failing to respond to treatment. Many hover between life and death for hours, and fully 25 per cent die in the course of subsequent relapses. Treatment however must not be given up too soon, for recovery may occur after protracted resuscitation.

Prophylaxis is the key note in asphyxia, and this depends on better obstetrics. If this can be accomplished there will be a considerable decrease in the incidence of stillbirth, early neonatal death and morbidity, above all reduction in the frequency of premature births, one of the most common causes of asphyxia. Careful pelvic mensuration will give indications for Cæsarean section before it is too late. Prevention of the toxæmia of pregnancy, prompt recognition of placenta prævia, detachment of the placenta, prolapse of the cord, and eclampsia, are important factors. The temptation to hasten the delivery of the breech should be avoided, because it adds to the difficulty of delivering the after-coming head. Protracted labours should be avoided. The utmost thought and care are required in the use of pituitary extracts, opiates, hypnotics, analgesics, and anæsthetics at the time of delivery. So often one of these is the cause of the asphyxia. In spite of all precautions there will still be cases to be treated.

The difference in treatment between asphyxia livida and pallida is one of degree. Simple measures suffice with the livid form, whereas more energetic treatment is necesary with the pallid type. The main essentials in either are, to keep the infant warm, to remove obstructing material from the air passages, and to prevent injury.

Immediately after birth there is usually a lull before breathing begins, during which time the carbon dioxide of the blood is increased to a degree sufficient to stimulate the somewhat sluggish respiratory centre. If the cord pulses strongly this may continue long enough, a minute or more, to become alarming. Instead of making efforts to stimulate respiration, the lull furnishes the doctor with a splendid opportunity to milk the trachea and aspirate mucus and amniotic fluid from the upper air passages, and thus prevent obstruction or aspiration. At the same time possible trauma from resuscitation may be avoided. When there is no effort to breathe, cord pulsation is weaker and cyanosis deepens, then the infant should be stimulated by rubbing or gently slapping it and cutting the cord. It is permissible to flick a few drops of cold water or ether on to the skin, but immersion in a cold bath is bad treatment. A deep breath or two followed by a lusty cry is the usual consequence of such stimulation. If the cry is not forthcoming and respirations are shallow and irregular, oxygen or, better, a mixture of 5 per cent carbon dioxide and 95 per cent oxygen should be administered. A few whiffs of aromatic spirits of ammonia are also of value in causing deeper respirations. If the infant seems lethargic from the use of narcotics, analgesics, and general anæsthetics, inhalations of the gases should be continued. In such instances the hypodermic administration of 1 to 1½ gr. of caffein sodium benzoate may have a prolonged stimulative action. One c.c. of alpha-lobeline injected intramuscularly or into the umbilical vein is of questionable value, but is worth trying when other methods are not available. The infant who does not respond to such treatment or who shows characteristic signs of asphyxia pallida is in need of gentle artificial respiration.

Repeated attacks of cyanosis suggest the possibility of pressure upon the respiratory centre from intracranial hæmorrhage. Release of pressure by cisternal or lumbar puncture, together with intramuscular injections of whole blood, are worthy adjuncts to the usual treatment of asphyxia.

After an infant has been successfully resuscitated it should be watched closely, for many times the lungs have not been sufficiently expanded to prevent recurrence of symptoms. Repeated inhalations of carbon dioxide and oxygen during the first few days are of undoubted value in reducing the incidence of partial atelectasis and pneumonia.

Hæmorrhagic disease of the newborn. — One feels a little insecure in discussing this subject after reading some of the recent literature. Doubts have been raised as to the true definition of this disease and as to whether some of the hæmorrhages in the newborn should be included under this head. With the discovery of vitamin K the etiology of this condition may be a little clearer. This vitamin is fat-soluble, and is found in alfalfa, an important constituent of pablum, in kale, spinach, tomatoes, cabbage, some vegetable oils, and hog's liver. It can now be obtained in capsules. In the first four days of life the coagulation time of blood is longer than for the period immediately following. This is due to the low level of prothrombin in the blood at this time. In hæmorrhagic disease of the newborn the increased coagulation time and decreased prothrombin level are exaggerated. With the administration of vitamin K the prothrombin level is increased and so the coagulation time is decreased.

The incidence of this disease has been falling considerably in the past decade. This may be due to the improved pre-natal care of the mother. Her diet is high in practically all the vitamins and minerals, and it is quite likely that the vitamin K intake is much higher than it used to be.

The signs appear on the third or fourth day of life, usually, but may be as early as the second or as late as the fifth day. Hæmorrhage may be from the nose, mouth, ears, eyes, cord, or bowel. Bleeding may also occur in the lungs, suprarenal glands, or into other viscera, and the body cavities. Hæmorrhage from the kidney, as shown by bloody urine, is rare. The general appearance of the infant is often that of a severe anæmia, the severity depending on the site and extent of the hæmorrhage. Blood examination shows an anæmia of varying degree and usually, but not always, an increased bleeding and clotting time. The prothrombin level of the blood has been found to be lowered considerably. With newer methods prothrombin levels can be determined without much difficulty. The normal clotting time, as measured by the capillary tube, is about five minutes. In this condition it may be prolonged to ten minutes or more. The bleeding time is normally less than the clotting time.

The prognosis depends on the source of the hæmorrhage, the promptness of diagnosis, and the treatment. Hæmorrhages into the lungs, adrenals, and body cavities are the most serious.

Until the last year the generally accepted treatment has been the injection of blood intramuscularly or intravenously. A blood transfusion of 50 to 100 c.c. was the treatment of choice in the severe cases, while 20 to 30 c.c. of whole blood injected deeply into the buttocks sufficed for the milder ones. Occasionally in the serious cases the transfusion was repeated in 24 hours. Mother's blood was most often used, although the father's is of more value. With the introduction of vitamin K it may be that the use of blood injections will be limited to those cases with severe loss of blood. However, until further work is done blood should be used with the aid of vitamin K. The dosage of vitamin K is still uncertain, roughly 1,000 chick units every 4 hours, four to six times daily, for two to four days. Since it has been shown that the prothrombin level in the newborn can be appreciably elevated by the administration of vitamin K to the expectant mother, it may be worth while to give it regularly for a period before parturition.

Intussusception.—This is the acute abdominal condition most peculiar to the child. As in appendicitis, early and accurate diagnosis determines a low mortality, and again it is the typical case that is not recognized.

For the most part only infants are affected. Intussusception occurs most frequently between the ages of six months and two years, and in particular from the seventh to the ninth month. The incidence in boys is about three times that of girls, and the victim is usually in the best of health. The vast majority of intussusceptions begin at the ileocæcal valve or in the lower six inches of the ileum. A small number begin at other points in the large or small bowel.

The essential clinical features are violent abdominal pain, vomiting, the passage of blood and mucus from the bowel, and the presence of

the characteristic tumour. The onset is sudden, the infant screaming and drawing up his legs. Vomiting may occur. The attack lasts only a few minutes and then subsides, leaving the baby limp and pale. Further attacks occur at intervals, each attack becoming more protracted and severe. Normal stools may be passed at first, but soon they become loose, green, and mucus and blood may be seen, the so-called "red currant jelly" stool. The abdomen is soft between attacks, and the sausage-shaped "tumour" is usually noted somewhere along the colon. On examination the rectum is found to be empty except when the head of the intussusception has reached that distance. When the finger is removed blood-stained mucus usually follows. X-ray help is only required in the rare case presenting difficulty in diagnosis. In the average case a barium enema may be dangerous and take up valuable time. If the diagnosis is not made in 12 to 24 hours the infant becomes toxic, the pulse increases, the temperature may rise, and signs of peritonitis may appear.

The earlier the diagnosis and institution of treatment, the better the prognosis. Even with successful reduction toxæmia may be a serious factor. The average mortality is given about 50 per cent. There seems to be little excuse for such a high figure if this condition is kept in mind when one is called to see an infant in this age-group with an abdominal pain.

Laparotomy and reduction is the only safe method of treatment. In the past abdominal massage, rectal injections under a fluoroscope have been tried. These methods are practically always useless, and may be dangerous.

Infantile tetany.—This is not an infrequent cause of convulsions in the second six months of life. It is practically always associated with mild rickets and is due to a low blood calcium content. It has been seen occasionally in the first few weeks of life, and its incidence diminishes quickly after the second year. As in rickets, tetany usually occurs in the spring, following the absence of the ultra-violet rays of the sun. It is much more common in males than females. Diets low in calcium are conducive to tetany, whereas adequate vitamin D is a sure prophylactic. Premature infants are more prone to this condition. Infections often will precipitate convulsions when latent tetany is present.

The symptoms are convulsions, carpopedal spasm, and laryngospasm. Convulsions are the commonest sign and may be the only one in the young infant. They are usually generalized, may come on intermittently, or be almost continuous. Between convulsions the infant is mentally alert. Unless associated with an infection there is no fever. Carpopedal spasm, which affects the muscles of the hands and feet, is sometimes the only symptom in the older children. It may be quite severe and painful. The spasms may be intermittent or continue for hours without intermission. Laryngospasm is characteristic of tetany and occurs chiefly in young infants. It is a spasm of the laryngeal muscles, and on deep inspiration there is a peculiar crowing sound. Occasionally the spasm may be severe enough to cut off respiration and cause sudden death.

In addition to the above symptoms the following three signs may be elicited. (1) Chvostek's sign. To elicit this the infant must be quiet. On tapping the facial nerve anterior to the ear a contraction of the muscles about the mouth, nose, or eye on the same side of the face is elicited. (2) Trousseau's sign. By compressing the upper arm with a tourniquet with a pressure between diastolic and systolic a spasm of the fingers and hand develops. (3) Erb's sign. This requires the use of a galvanic current. With the kathode at the wrist it is noted that an abnormally small current will cause a contracture of the thumb or fingers. The laboratory gives the most conclusive sign in the estimation of the blood calcium. Normally, this figure is fairly constant around 10 to 11 mg. per 100 c.c. of blood; in tetany this level is reduced to 6 or 7 mg. or lower.

With prompt diagnosis and good treatment the prognosis is usually good. If the convulsions are violent and often repeated, or if accompanied by infection, death may occur. Death has occurred with laryngospasm, and sometimes suddenly without obvious explanation from cardiac or respiratory failure.

Prophylactic treatment is of the most importance. With an adequate intake of vitamin D throughout the fall, winter, and spring months, and direct exposure to the sun's rays in the summer this condition cannot occur. To control the convulsions chloral hydrate is the drug of choice. This may be accompanied by morphine in the severe cases. Chloral hydrate

may be given by rectum if it cannot be given by mouth. The dosage is 3 to 5 gr. for an infant under 6 months; 5 to 10 gr., if over 6 months. The dosage of morphine is about 1/70 gr. per 10 pounds of body-weight, and can be repeated in safety after 4 to 6 hours. If the convulsions cannot be controlled by these methods ether may be inhaled, and if this fails avertin rectally is effective. Sedatives may be necessary to relieve the pain of other milder forms of spasms, particularly laryngospasm. Calcium chloride is the most effective of the calcium salts in raising the blood calcium. It should be given by mouth without delay as soon as tetany is diagnosed or suspected. When active tetany is present an initial dose of 45 to 60 gr. should be given, preferably in a 10 per cent solution, and by gavage if necessary. This should be followed by 15 gr. doses at 4 to 6 hour intervals for the first 24 hours. After that 15 gr., three or four times daily, will keep the symptoms under control. This should be continued for at least two weeks, while antirachitic treatment is getting under way. In the milder forms of tetany it is not necessary to start with such a large initial dose. Because of the bitterness of calcium chloride it is best given in milk. Calcium lactate is less effective than calcium chloride, but may be used when the chloride is poorly tolerated. The dosage is double that of the chloride.

Scurvy.—Sporadic cases of scurvy still turn up occasionally in spite of the widespread knowledge of the value of orange juice and tomato juice in the infant's diet. The diagnosis is easily made, but not infrequently missed. In taking a history, inquiry should always be made regarding the intake of orange juice or tomato juice. So often the fruit juice will be omitted because the baby chokes, or it seems to cause diarrhœa, or it develops a rash.

Due to the relatively high content of vitamin C in breast milk, as compared with cow's milk, infants while on the breast do not develop scurvy. What vitamin C there is in cow's milk almost all disappears with age, pasteurization, and boiling. In the majority of cases symptoms appear between the ages of 8 and 13 months. Over 18 months and under 6 months scurvy is most unusual.

Tenderness and swelling of the legs, swollen and bleeding gums, generalized tenderness, and irritability are the commonest symptoms. Crying usually results when the infant is moved or an attempt is made to have him sit up or stand. Retardation of gain in weight, or even loss of weight accompanies the condition. Minute or gross hæmorrhages may occur as follows: petechial hæmorrhages in the skin, bruised areas on the extremities and face, swelling of the eyelids with black and blue spots, protrusion of one or both eyes from orbital hæmorrhages, nosebleeds, vomiting of blood, blood in the stools or in the urine. Usually there is a slight rise in temperature and pulse. The position of the patient is characteristic, varying with the intensity of the disease. Osteoporosis, elevation of the periosteum, cortical atrophy, intensification of the zone of preparatory calcification, a zone of rarefaction just shaftward of this, are some of the features.

The prognosis is excellent provided treatment is given before infections develop.

Within the first month of life orange juice should be started. This is especially valuable in the artificially fed infants. If for any reason it cannot be taken tomato juice or ascorbic acid may be given instead. The dose of orange juice should be 1 to 2 oz.; of tomato juice 2 to 3 oz.; and of ascorbic acid 25 mg.

Treatment consists in giving 3 oz. of fresh orange juice daily in single or divided doses. It may be diluted or sweetened, and if refused may be gavaged. Ascorbic acid, 100 mg. daily, is quite as good if there is difficulty in giving orange juice. As soon as the symptoms have disappeared the dose of juice and ascorbic acid may be diminished to the prophylactic level.

OXYGEN REQUIREMENTS FOR PILOTS.—An airplane pilot who is not provided with oxygen begins to lose his mental and physical efficiency at an altitude of about 12,000 feet, Harry G. Armstrong, Toronto, Can., states in *Hygeia, The Health Magazine.* His symptoms are more pronounced at 18,000 feet. Between 18,000 and 22,000 feet his actions are like those of a drunken man, and he becomes either sleepy or very active with outbursts of laughter or rage. At about 25,000 feet unconsciousness occurs and unless descent to a lower altitude is made death results within a few minutes.

CÆSAREAN SECTION*

BY DONALD M. LOW

Toronto

THIS report is based on a survey of the Cæsarean sections performed in the public wards of the Burnside division of the Toronto General Hospital during a fifteen year period, 1925 to 1939 inclusive. It is felt that a study of the results obtained is of value as representing an average cross section of obstetrical difficulties for which a small group of specialist attending staff have used Cæsarean section. The experience of this staff has been gradually and sometimes painfully acquired, but the lessons learned have undoubtedly resulted in improved results which should be capable of transference to those not having the same opportunity of observing such a large series of cases.

TABLE I.
1925 TO 1939
CÆSAREAN SECTION SUMMARY

Deliveries	*Sections*	*Incidence percentage*	*Maternal mortality percentage*	*Fetal and neonatal mortality percentage*
11,527	343	2.97	3.79	17.2

In the fifteen-year period under review I have excluded all deliveries prior to the age of viability where section would not likely play a part. As a result our incidence rate of section is based on an unusually severe standard. In this fifteen-year period 11,527 cases were delivered, amongst which there were 343 sections, giving a 2.97 per cent average incidence of section for the whole period. This average compares favourably with other series, and the yearly incidence ranged from a low of 1.75 to a high of 5.78 per cent; and, as the entire series naturally divides into three periods of five years, we find that the average incidence for the last five-year period was 2.26 per cent. It is our hope that we can maintain our incidence of section from now on below 3 per cent and not show such wide variation from year to year as 1.75 to 5.78. One must recognize that there is bound to be considerable yearly variation, but we feel that an average for a five-year period should be maintained at or below the level of 3.0 per cent.

TABLE II.

	High percentage	*Low percentage*	*Porro percentage*
1925 to 1929	51.4	39.1	9.5
1930 to 1934	35.7	50.0	14.3
1935 to 1939	37.6	54.8	7.6

TYPE OF SECTION

The type of section performed has been either the so-called high or classical, the low cervical, and the Porro hysterectomy. As in Table II the type of section has been summarized for the three five-year periods. It is interesting to note that Porro section has been performed on an average in about 10 per cent of the whole series, and for the individual five-year periods has varied somewhat above and below this average. It would appear that the relative position of high and low section has been gradually reversed, in that we are tending to employ low section more often than high. We are still however reserving a definite place for high section. It is important to realize that each type of section has a field of usefulness. More important still is it to understand better that each has its limitation. It is undoubtedly true that on many occasions the classical or low cervical section is done when Porro section would be better, just as vaginal deliveries even by craniotomy would no doubt produce less risk on some occasions where Porro section is chosen. The greatest difference of opinion seems to have arisen since the advent of low cervical section as to the relative merits of this type and classical section. Surely sufficient experience has been gained that we can admit the limitations and usefulness of each, rather than become such ardent advocates of one to the entire exclusion of the other. The most ardent advocate of classical section must admit that in certain situations low cervical section has distinct advantage. Is it too much to ask those favouring routine employment of low cervical section if classical section sometimes does not offer distinct advantage, or at least no greater

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risk? I believe it is true that each type of section has a particular field of usefulness and that it is possible to outline the usual situations in which each type can best be employed.

Classical section can well be employed in cases of election not in labour or very early in labour where the membranes are still intact and no vaginal manipulations have taken place. Uncomplicated cases of placenta prævia are also sometimes easier to deal with by classical section.

Low cervical section is preferable for cases in labour, preferably where the membranes are still intact or not ruptured longer than 12 to 24 hours, or following a satisfactory test of labour with a minimum of vaginal examination or manipulation, and where the evidence does not point to the presence of gross sepsis.

The indications for Porro section are relatively few, namely, neoplasm, ruptured uterus, severe cases of accidental hæmorrhage and potential sepsis in labour.

TABLE III.
INDICATION SUMMARY

	Section	*Percentage*	*Type of section*			
			H.	*L.*	*P.*	*E.P.*
Disproportion	118	34.4	36	76	4	2
Previous section	83	24.2	31	51	1	
Placenta prævia	41	11.9	34	6	1	
Heart disease	37	10.7	21	12	4	
Toxæmias	25	7.2	13	7	5	
Accidental hæmorrhage	11	3.2	2	2	7	
Tumour	6	1.7	1	0	5	
Ruptured uterus	5	1.4	0	0	5	
Miscellaneous	17	4.9	8	7	2	

INDICATIONS

As shown in Table III the reasons given for section show that the main indications come under comparatively few headings. As usual in a survey of this kind cases of *disproportion* head the list with 34.4 per cent, and as *previous section,* with 24.2 per cent, comes next frequently, we might consider that roughly more than half of the indications for section come under the heading disproportion because of the fact that so many previous sections had been done for that reason. Placenta prævia, with 11.9 per cent, comes next in order, and in almost every instance high section was preferred in this condition. Heart disease was the indication in 10.7 per cent, but these cases were all operated on during the first five-year period since which time we have not performed Cæsarean section for heart disease alone in a single instance. Results of conservative treatment of heart disease by vaginal delivery, apart from obstetrical indication, seem to be as good as by Cæsarean section and therefore heart disease is not considered in itself as an indication for section. Toxæmia was the indication in 7.2 per cent but never where convulsive seizures had occurred. Although accidental hæmorrhage was the indication in 3.2 per cent it is becoming less frequent an indication, and only for the most severe cases, as illustrated by the fact that 7 out of the 11 cases were Porro sections. There were among the remaining indications 6 cases operated on because of tumour, 5 cases of ruptured uterus and 17 cases classed as miscellaneous indications in nearly half of which the section was performed mainly for the purpose of sterilization at the time of operation.

Cases of disproportion comprise by far the largest indication for section. Where the disproportion is obvious and extreme no test of labour is usually necessary. But it is in the so-called "border line" case, where a test of labour is necessary, that careful management is most important. How long the test is to go on depends on a great many factors, but on an average a test of 6 to 12 hours with satisfactory labour pains should be sufficient to enable one to make the decision as to proper method of delivery. During this period no vaginal or, at the most, one careful vaginal examination should be all that is necessary to supplement information that can be obtained by rectal examination. Intake of fluids should be kept up by mouth or intravenously if necessary, and rest obtained by the judicious use of a sedative, so that, if the decision is made to proceed with section the condition of the patient is satisfactory. If further labour and delivery by the vaginal route is decided upon the patient is all the better for such careful treatment. We will find the greatest mortality in those cases where the general condition of the patient has been lowered beyond the point of safety by exhaustion or ill-advised manipulations. The danger signals in such cases are increased pulse rate, pyrexia, dehydration, general restlessness, anxious expression, and increasing abdominal distension. These symptoms will arise in a test of labour where proper care of the patient is not given. This can be avoided by the proper use of a sedative, administration of fluids, and a minimum of vaginal examination or manipulation. In other situations, already prejudiced by hæmorrhage, sepsis, toxæmia, cardiac, or constitutional disease, every effort should be made

to improve the condition of the patient before deciding on section.

"Once a section always a section" has been a dictum more or less adhered to by most authorities. In general, I believe it to be a safe rule, but exception to it may sometimes be made in a patient who has had other vaginal deliveries prior to a section from which resulted a normal convalescence. Even in these careful watch must be kept and severe second stage pains avoided by means of the forceps. It follows from the above dictum that the original decision of the necessity for Cæsarean section in any case should depend on a very definite indication. This further emphasizes the very great responsibility of him who makes the decision for the first section.

Placenta prævia of the central or complete type calls for section if at all possible. Most authorities agree on this, but for the marginal and lateral types there is room for considered opinion of each case. The decision to do a section in these latter cases depends mainly, I believe, on the relation of the presenting part to the brim and cavity of the pelvis. If the presenting part is in the cavity or can be forced by pressure above the pubes into the brim vaginal delivery can usually be safely accomplished.

The place for section in cases of *accidental hæmorrhage* should not be a prominent one, but reserved only for the occasional acute fulminating type with such severe hæmorrhage and extensive damage to the uterine musculature that no sign of labour can be observed. Occasionally, in less severe cases, it will be admitted that the importance of fetal salvage will necessitate section.

Cases of *heart disease* without failure or obstetrical indication are as a rule best treated conservatively. In cases with failure every effort should be made first to combat the failure, but, if improvement does not occur, the decision becomes extremely difficult as, no matter what method of delivery is decided upon, a disastrous result is likely to occur. Generally speaking, all cases of heart disease not complicated by other obstetrical difficulties are best treated conservatively.

In the treatment of *toxæmia* the use of Cæsarean section is restricted to those acute fulminating cases in the pre-eclamptic phase where, in spite of treatment, the toxæmia is rapidly progressing. In these it is felt that speedy delivery seems vital rather than the comparatively arduous delay of an induced labour. It is only rarely that such toxæmia alone is an indication for section. As a general rule, where no other obstetrical difficulty exists, cases of toxæmia are best treated conservatively with or without induction of labour. All are now in agreement that Cæsarean section is contraindicated in the patient with convulsions.

Occasionally dystocia apart from the bony pelvis may occur from *fibroids, ovarian tumours,* or *malignant disease of the cervix.* These are all usually diagnosed without difficulty. It is rare that one finds ovarian tumours the cause of any real dystocia. The low-lying intramural or subserous fibroid situated posteriorly and filling up the pouch of Douglas, if it does not elevate itself or cannot be pushed well up above the presenting part, is an absolute indication for delivery by Cæsarean section. Carcinoma of the cervix is very seldom encountered accompanying pregnancy, but, when it does, one may expect only to recover a living child by section as the outlook for the mother is usually without hope.

Ordinarily, Cæsarean section is not done solely in the interests of survival of the child although it must be admitted that occasionally a situation will arise where, the prospect of further pregnancies being remote, section will be undertaken so that a living child may be assured. In such instances, the safety of the mother remains paramount, and if any real maternal contraindication to section exists the operation should not be done. The conscientious obstetrician will accept the possibility of still-birth rather than submit his patient to undue risk.

The foregoing, I believe, constitutes a survey of what should be considered the main indications for Cæsarean section. Only by strict adherence to this comparatively small number of indications and a refusal to admit the very numerous other reasons sometimes given can we, as obstetricians, demonstrate our belief that too free enlargement in scope of the indications for section is one of the main causes of mortality of Cæsarean section.

If we exclude heart disease, which has not appeared as an indication for section in this series for the past ten years, we can say that the indications for Cæsarean section should fall under relatively few headings, namely, disproportion, previous section, placenta prævia, toxæmia, accidental hæmorrhage, tumours of

bony pelvis or soft parts, and ruptured uterus.

Parity and age incidence.—Of the 343 sections, 117 are listed as primigravidæ, the remaining 226 being more than one gravida. The average age of the whole series was 29.5 years. The youngest patient operated on was 16 years and the oldest 49.

Sterilization. — Including 34 Porro sections there were in all 149 sterilizations performed in the series of 343 sections. This gives a percentage sterilization of 43.4.

Stay in hospital.—The period of hospitalization gave the average story as follows: classical section, 18.8 days; low cervical, 21.5 days; Porro, 29 days. These figures do not include cases of heart disease, the average stay of these cases being 27 days in the obstetrical ward prior to transfer to the medical ward.

TABLE IV.
MORBIDITY

	99–100	100–101	101–102	102
Classical ...	68	39	12	10
Low	63	42	15	14
Porro	13	9	3	8
	144	90	30	32

There does not seem to be any standard of morbidity in reports of Cæsarean sections. Here are recorded all cases with elevations of temperature above 99°, even if not consecutive readings, which occurred on more than one single occasion. This grouping shows that 152 cases, or 44.0 per cent of the whole series, showed temperature readings above 100°.

TABLE V.
NON-FATAL COMPLICATIONS

	Classical	*Low*	*Porro*
Phlebitis	4	6	2
Wound infection	6	12	1
Pyelitis	1	6	1
Pelvic hæmatoma	0	2	0
Pelvic cellulitis	0	1	0
Pelvic abscess	0	0	1
Pneumonia	1	1	0

A study of the non-fatal complications shows, wound infection, phlebitis and pyelitis as the most common in order of frequency.

Still-births and neonatal deaths.—There were 41 still-births (11.95 per cent) and 18 neonatal deaths (5.25 per cent), giving a gross fetal mortality of 17.2 per cent. The still-births for the most part were due to prematurity, accidental hæmorrhage, ruptured uterus, placenta prævia, and fetal deformities.

TABLE VI.
MATERNAL MORTALITY

	Sections	*Deaths*	*Rate percentage*
High	146	3	2.15
Low cervical	161	4	2.48
Porro	34	5	14.70
Ex. P.	2	1	50.00
	343	13	3.79

In the series of 343 sections there were 13 maternal deaths, giving an uncorrected maternal mortality of 3.79 per cent. In this particular series the mortality rate for high section was 2.15 per cent, for low section 2.48 per cent, and for Porro section 14.70 per cent.

ANALYSIS OF THE FATAL CASES

1. Classical section — 3 deaths. All three deaths resulted from general peritonitis. In two cases, one of disproportion complicated by a very severe secondary anæmia and the other of central placenta prævia, also complicated by severe primary anæmia, the patients were very poor pre-operative surgical risks, and it is likely that any method of delivery would have resulted in a fatality. The remaining death was due to a serious breakdown of operating-room technique in a case of fibroid tumour causing dystocia.

There have been no deaths from classical section during the past seven years. During this time 49 such sections have been done.

2. Low cervical section—4 deaths. Two deaths from pulmonary embolism, one in a case of rheumatic heart disease, and the other a second section of election; one death from pneumococcal peritonitis in an elderly primipara with marked disproportion, complicated by respiratory infection; the remaining case was a repeat section of election and the patient died of unexplained peritonitis on the 10th day. There have been no deaths from cervical section during the past five years. During this period 51 such sections have been done.

3. Porro section—5 deaths. There were two deaths in severe cases of accidental hæmorrhage, one from shock within 24 hours, and the other of peritonitis and intestinal obstruction. One death occurred in a neglected case of disproportion admitted to hospital in a very exhausted state; one death in a case of ruptured uterus admitted to hospital, also in a very exhausted state. The remaining death occurred in a patient critically ill with acute pulmonary œdema complicating a severe pre-eclamptic toxæmia

where any method of delivery would almost certainly have resulted fatally.

The last deaths from Porro section were the only two deaths occurring in the 93 sections of all kinds performed during the past five years.

4. De Latzko section—1 death. The death from De Latzko section occurred in an exhausted and infected patient where craniotomy might better have been employed.

A consideration of these 13 maternal deaths shows that 9 died of peritonitis, 2 of pulmonary embolus, 1 of cerebral thrombosis, and 1 of shock and cardiac failure. The primary mortality following all types of Cæsarean section will include the usual minimum surgical mortality attending all laparotomies. There will be as well the unavoidable obstetrical mortality in critical situations where it is possible that any form of delivery may result fatally, but where it is felt that the use of Cæsarean section offers the patient the best chance of survival. Where such serious situations arise it is possible that craniotomy might be more generally employed in certain cases in which the tendency seems to be to choose the somewhat easier method of Cæsarean section in spite of grave contra-indications.

CONCLUSIONS

1. The indications for Cæsarean section are relatively few.

2. Each type of section has definite indications for employment.

3. *The mortality from all types of section is mainly due to unfavourable pre-operative conditions.*

4. Careful selection of patients for operation is more important than the selection of the type of section.

5. Consequent upon this the more frequent use of craniotomy in neglected or unfavourable cases, where Porro section is the alternative, is advisable if the mortality is to be reduced.

RÉSUMÉ

Sur 11,527 accouchements survenus en 15 ans, 343 césariennes ont été pratiquées, soit 2.97 pour cent du total, avec une mortalité de 3.79 pour cent pour les mères et de 17.2 pour cent pour les fœtus et les nouveau-nés. Trois procédés furent utilisés: la section haute, la section basse et l'opération de Porro; la première pour les cas à travail débutant, la seconde quand le travail était assez avancé, et la dernière, moins souvent, dans les cas de tumeurs, de rupture utérine ou d'hémorrhagie. Les indications de la césarienne sont peu nombreuses. Les principales sont la disproportion cranio-pelvienne, les césariennes antérieures, le placenta prævia, les toxémies graves, excluant les convulsions éclamptiques, les tumeurs obstruant le détroit supérieur, les hémorrhagies accidentelles et les ruptures utérines. Les cardiaques sont graduellement éliminées du cadre des indications de la césarienne. Les complications non-mortelles furent l'infection de la plaie, les phlébites et les pyelites. C'est l'opération de Porro qui greva le plus fortement la statistique. L'état pré-opératoire déjà mauvais est la grande cause de mortalité, et dans de meilleures conditions le pourcentage devrait être inférieur à 3 pour cent.

J. SAUCIER

PREVENTION AND TREATMENT OF LACHRYMATION*

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THE term lachrymation literally means the secretion and discharge of tears. Its use in this paper, however, is in a more general sense not only including tear secretion but also epiphora, an abnormal overflow of tears down the cheek mainly due to obstruction of the lachrymal passage. We shall therefore consider the subject of lachrymation not only from the point of view of secretion but also from that of drainage.

In considering the treatment of lachrymation due to increased tear secretion, it will be helpful to review briefly the nerve supply to the lachrymal gland which, with its accessories, is responsible for the secretion. Three nerves are involved, namely, the 5th and 7th cranial nerves and the sympathetic. The 5th supply is through the lachrymal nerve which enters the gland with the blood vessels and anastomoses with the zygomatic branch of the second or maxillary division. The 7th nerve fibres reach the gland through rather a long course. The greater superficial petrosal nerve leaves the geniculate ganglion of the facial nerve and joins the deep petrosal nerve arising from the carotid plexus of the sympathetic, to form the Vidian nerve which enters the sphenopalatine or Meckel's ganglion. From here there is doubt as to the course of the facial fibres. Some state that they enter the zygomatic branch of the maxillary

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nerve mentioned above and enter the gland through the lachrymal nerve. Kalt[7] does not hold with this view, as the zygomatic branch leaves the maxillary nerve before the fibres from the sphenopalatine ganglion enter it. A more likely course is through the temporomalar branches. The sympathetic nerve supply is derived from the carotid plexus and accompanies the lachrymal artery. Other branches may reach the gland from the sphenopalatine ganglion. Although the nerve supply is thus well known, the course of the secretory impulses is not by any means well understood. It is probable that the 5th nerve is an afferent pathway; that the sympathetic causes the ordinary amount of lachrymal secretion; and that the facial nerve is responsible for the excessive flow.

Stimulation of the 5th nerve as an afferent pathway explains the tearing that occurs in lesions of the cornea or conjunctiva or irritation within the nose, apart from direct blockage of the nasolachrymal canal which will be considered later. Irritative lesions of the 7th nerve and of the sympathetic likewise cause increased tear flow, and destructive lesions diminish the flow. Nevertheless, the lachrymal gland continues to secrete even after all the nerve supply to the gland has been divided. This occurred in one of our patients. He had had various operative procedures performed by Dr. W. V. Cone to relieve the persistence of severe pain due to right-sided 5th nerve neuralgia. Dr. Cone performed a partial section of the 5th nerve through the subtemporal approach, resection of the greater superficial petrosal nerve through the same approach, complete section of the 5th through the occipital approach, removal of the superior cervical sympathetic ganglion, and, finally, section of the glossopharyngeal nerve, and the 2nd, 3rd, and 4th cervical nerves on the right side. In spite of this, tears are still present in the right eye and the cornea has remained normal for the last one and a half years.

Tearing is one of the commonest complaints in ophthalmic practice. Its treatment necessitates a careful history of the complaint in addition to the routine inspection of the lachrymal apparatus, as well as of the conjunctiva and cornea. If the tearing is of sudden onset a foreign body or an inverted lash may be found wiping the cornea or conjunctiva, and its removal gives immediate relief. Usually the complaint is of longer duration, however, and greater difficulty is experienced in its treatment. Probably the commonest cause is chronic conjunctivitis from any of its various causes, such as conjunctivitis secondary to dacryocystitis, vernal catarrh, allergy, and mechanical irritation from trichiasis, districhiasis, and the like. In this condition, as well as in lesions of the cornea, it is obvious that the treatment be directed toward the lesion causing the conjunctivitis or keratitis rather than to the tearing itself. The same holds true for reflex tearing from irritative conditions within the nose, as impaction of the turbinate or areas of hyperæsthesia. These causes are usually discovered after all those in the eye itself and lachrymal apparatus have been ruled out. The tearing disappears on relief of the nasal condition.

The conjunctiva seems to become more sensitive to cold as age advances and tearing frequently is complained of about the time of the onset of presbyopia. Relief here is difficult, and if the lachrymal apparatus is not at fault we rely on some form of astringent drops, or in severe cases on operative interference which will diminish the flow of tears. This will be described later. Another form of reflex tearing is that which occurs through the optic nerve, as when looking at the sun or a bright light, especially when coming from places of less intense illumination. This has established a growing fad for various types of tinted lenses. The use of these for constant wear should, I think, not be encouraged, as tinted lenses, in my opinion, have a limited use, save as they are indicated in pathological states and harmful degrees of illumination.

Psychical weeping, which is peculiar to man and which is subservient to the emotions, does not come within the scope of this paper nor does the lachrymation associated with yawning, coughing or vomiting. It is interesting, however, that the newborn infant does not weep psychically, although the lachrymal gland is well developed, and, according to Roemer,[11] will secrete as a result of reflex irritation.

We shall now consider the normal disposal of tears and the treatment of various conditions which interfere with it and cause epiphora. Normally, the tears are swept across the cornea by the act of winking. In this the lower lid remains practically stationary while the upper one descends to meet it. This meeting takes place first at the outer canthus and proceeds inward as a wave to the inner canthus where

the excess fluid is picked up by the puncta. An accurate meeting of the lids is necessary to prevent overflow. The posterior border of the lids must be in apposition with the globe and the angle formed by the conjunctival surface of the lid and the intermarginal space must have a sharp edge. Rounding of this angle does not allow an even film of tears and epiphora is likely to be present. Similarly, notching of the lid margin, especially the lower one, frequently causes overflow. The puncta must be in a proper position to catch the tears in the lacus lachrymalis, and the canaliculi, lachrymal sac and nasolachrymal duct must be patent.

Lesions of the facial nerve with paralysis of the orbicularis palpebrarum muscle cause loss of the act of winking and this allows the tears to form in a lake along the lower lid so that they frequently overflow. Protecting goggles with close fitting sides, as those described by Adson and Schroeder,[1] or MacDonald,[8] are not only helpful but essential during the period of recovery. When the paralysis of the facial nerve is permanent, grafts which bridge the damaged portion, or grafting of the peripheral portion of the damaged nerve to one of the other motor nerves, such as the hypoglossal, usually improve the action of the orbicularis, and with it there is a corresponding improvement of the lachrymation.

Another type of lachrymation may occur following facial nerve lesions. This is seen chiefly in cases of Bell's palsy without complete recovery, and is known as the "crocodile tear" syndrome. According to Duel,[4] from 15 to 20 per cent of cases of Bell's palsy fail to recover completely, and of these, Tumarkin[12] says 80 per cent show crocodile tears to a greater or lesser extent. This consists of a troublesome epiphora which occurs during mastication. Tumarkin suggests the cause; that with the downgrowth of new fibres in the facial nerve some are diverted and find their way to the wrong muscle or gland. Thus, fibres intended for the parotid gland are diverted to the lachrymal so that during mastication the salivary nucleus is also bombarding the lachrymal gland with secretomotor stimuli. It is obvious that the only means of reducing the secretion would be removal of the lachrymal gland.

Notching of the lid border, especially of the lower one, often allows an overflow of tears. This notching is usually caused by lacerations of the lids or by injury during the incision and curetting of chalazia which involve the intermarginal space. Here I should like to stress that when the continuity of the intermarginal space is broken every effort must be made to get perfect coaptation of the edges. Also when incising a chalazion, where it involves the intermarginal space, the posterior angle of the lid must not be injured. If notching is present and epiphora is troublesome the notch must be removed by some type of plastic operation. When rounding of the posterior border of the lid interferes with the conduction of the tears to the inner canthus it is usually associated with ectropion, either of the lid as a whole or of the lower punctum. In either case, lachrymation is a very pronounced symptom. Some type of plastic operation is necessary to correct the ectropion. This may involve any procedure from the insertion of sutures, or cautery punctures, to the use of flaps or grafts. In the senile cases I have found the Kuhnt-Szymanowsky operation very satisfactory.

When the lower punctum fails to be in the position to collect the tears from the lacus lachrymalis, provided the lachrymal canal is patent, a simple procedure usually gives most satisfactory results. The punctum is found to be separated from the lacus lachrymalis by the posterior border of the lid. It should be dilated first, but this is usually not enough. Then the point of one blade of a pair of fine scissors can be inserted through the punctum for about 2 to 3 mm. in a direction backwards and inwards and the scissors are closed. This causes an incision through the posterior border of the lid. With a pair of fine tooth forceps the posterior lip of the slit lid border is then grasped and is excised with the scissors. This produces a small funnel opening which gives permanent relief. Slitting of the canaliculus, other than in the above manner, is, to my mind, not only unnecessary but bad treatment, and should never be carried out except for the removal of concretions or tumours of the canaliculus. Even then the incision should be closed with sutures.

When there is an obstruction in the lachrymal passages its location should be determined. This is done by means of a small probe and the lachrymal syringe. A No. 1 or 2 Bowman's probe is passed along the canaliculus. If an obstruction is found here, and in my experience this is not infrequent, the probe can be forced into the sac and then withdrawn. If now on syringing the fluid escapes into the nose we know the obstruction is located in the canaliculus.

This may be a concretion which must be removed, or a stenosis which requires further probing. If, however, we reach the sac without difficulty, the obstruction is located in the nasolachrymal duct and the probe will then have to be passed along this canal into the nose. Many cases can be cured by careful probing and syringing. I have always used small probes, usually No. 2 Bowman's, but No. 4 can be passed without damaging the canaliculus. Often there is a recurrence but similar treatment may be carried out and in the end relief is often obtained. I have never used larger probes as I feel capillarity is lost by their use. The same applies to the use of stylets of all kinds. Various solutions for syringing the passages after probing have been recommended, but I have never experienced any benefit from them over that of sterile water or salt solution. An exception to the above treatment is in the atresia of the lower end of the nasolachrymal canal that occurs in the new born. This is usually cured by pressure over the sac, and it is only rarely that probing is necessary.

When dacryocystitis develops and is not relieved by probing and syringing, more radical operative interference is necessary. At one's disposal is some type of conservative operation or excision of the lachrymal sac. Chandler,[3] in an excellent paper, has enumerated the development of the conservative procedures in a chronological order, with complete bibliography up to 1936. My experience has been limited to the West operation and to transplantation of the lachrymal sac. The results, when favourable, are most satisfactory in that no epiphora follows. In spite of this, excision of the sac is still performed by a great many ophthalmologists. It has much to be said for it, in that the operation is easy to perform and requires but a few minutes to carry out. Moreover, the number of patients who complain of epiphora afterwards is small. Paparcone[10] found only four or five patients with troublesome epiphora in 302 cases of extirpation of the sac. I have always felt that in many cases, after a clean excision of the sac without injury to its periorbital walls, some tears must escape into the nose. Meller[9] has the same feeling. In older people, and in those distant from expert care, I feel that excision of the sac is the operation of choice; but in the young a conservative operation should be carried out.

If tearing be present after excision of the sac, as a rule, removal of the inferior lobe of the lachrymal gland gives satisfactory results. Division of the lachrymal tubules, as suggested by Jameson,[6] may be performed. I have not attempted this operation as I believe that the good results obtained in removal of the inferior lobe of the gland is due mainly to the incision of the tubules which must occur in this operation. The only structure liable to be injured in the operation is the aponeurosis of the levator palpebræ superioris, which lies between the orbital and palpebral lobes of the gland. I have excised the lower lobe of the lachrymal gland in patients with patent lachrymal canals but who complained of persistent tearing, and the satisfactory results have justified the operation. Probing lachrymal canals in patients with tearing but with free escape of fluid into the nose on syringing seems to me bad practice. I think it is better to attempt to reduce the secretion.

In patients with troublesome epiphora after removal of the lachrymal sac, Arruga[2] states that dacryostomy will relieve the tearing in two-thirds to three-quarters of the cases if the lower canaliculus is patent in its whole course. In this operation the opening in the nose is made opposite the inner end of the canaliculus and the edges are sutured to flaps of nasal mucous membrane. I have seen one patient on whom this operation was performed with satisfactory results.

Occasionally, in troublesome tearing where all other means of treatment have failed, excision of the orbital lobe of the lachrymal gland is to be advised.

An instance is that of J.St.L., aged 42 years, clerk, who had very troublesome tearing of both eyes for years. He gave a history that he had had some form of constructive operation performed on the right lachrymal sac with excision of the inferior lobe of the right gland, with no relief. He also had a chronic suppurative dacryocystitis on the left side. I removed the left sac and following this operation there was no epiphora in the left eye. One year later I removed a right inferior lobe of the lachrymal gland, but tears continued to trouble him. I then removed the orbital gland seven months later with immediate relief and the patient has been comfortable for the last year and a half. The sac was not interfered with, as no pus could be expressed and both canaliculi, which had been slit, were bound down in scar tissue.

Excision of the orbital gland is not difficult but it does not seem to have met favour. I believe, however, that it has a place, namely, that of a last resort.

The radical procedure of Holmes,[5] in which he removed the orbital gland at the time of excision

of the sac, has never been accepted because of the danger of infection and because of the realization that the operation was unnecessary as a routine procedure. When tearing is annoying and cannot be removed by any of the other means mentioned above, excision of the orbital gland, though radical, will relieve it with certainty.

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MENINGITIS OF THE NEW-BORN DUE TO PSEUDOMONAS AERUGINOSA

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SINCE Gessard[1] first demonstrated that the chromogenic micro-organism which he named *B. pyocyaneus* was the cause of "blue pus" it has been widely recognized as a cause of suppurative lesions of all parts of the body. Too frequently, however, it is dismissed as an unimportant secondary invader, or merely as a "contaminant". In general it is considered that the severity of the lesion depends upon the low resistance of the individual rather than upon the great pathogenicity of the micro-organism.

Epstein and Grossman[2] have presented a brief review of the literature of infections due to this organism in children, under the heading of skin, ears, eyes, bone, respiratory, digestive and genito-urinary tracts, meninges and general systemic infections. They concluded that infection of the skin is most frequent, that it is the portal of entry for septicæmia, and that there is a predilection for the umbilical wound in the new-born. They believe that infection of the meninges is rarely blood-borne, but arises usually by direct extension.

The first reported cases of meningitis due to *Pseudomonas aeruginosa* appear to be those of Ehlers.[3] A brother and sister, aged 11 and 12 years, suffered from generalized infections and meningitis. One died and the organism was isolated from the lesions and heart blood, but unfortunately the cerebrospinal fluid was not examined. Kossel[4] reported the case of a six-weeks old child in whom meningitis followed a middle-ear infection. A pure culture of *P. aeruginosa* was isolated from the pia and from the heart's blood.

When Evans[5] reviewed the literature in 1936 she was able to collect a total of 39 cases of meningitis due to this organism. She added 3 cases of her own. Shrewsbury[6] has reported an additional primary case, and a secondary case was reported by Roberts and Belsey.[7] Five of these cases occurred in the new-born.

In brief, the reported cases are nearly equally divided between primary and secondary cases, with a mortality rate of 50 and 75 per cent respectively. The primary cases have occurred chiefly in adults, many of them following routine lumbar puncture, the inference being that the organism was introduced during this simple operation. Secondary cases occur chiefly among children. One of these, reported by Benfey,[8] was in an 8-day old infant in whom the infection apparently gained entrance through the umbilicus. This is the probable entrance in the case which we shall report below. Gaucherand and Pigeaud[9] have reported a case of even more particular interest. Their patient, a 4-day old infant, was the offspring of a mother suffering from septic endometritis. They concluded the organism gained entrance from the amniotic fluid. As Epstein and Grossman have pointed out, the gastro-intestinal tract is frequently the site of infections due to this organism. Such infections often take the form of infantile diarrhœa, which is frequently fatal. Stewart and Bates[10] record a case of a middle-aged female

suffering from diarrhœa and severe anæmia. *P. aeruginosa* was isolated from the urine and fæces. These gastro-intestinal cases are referred to, since the infant concerned in the report below evidently acquired the infection from its mother who was suffering at the time of delivery from a severe enteritis and from whose fæces *P. aeruginosa* was isolated.

CASE REPORT

Mrs. C., an Indian woman aged 27 years, was admitted to McKellar Hospital, Fort William, on December 11, 1939, a patient of Dr. J. C. Gillie. Her chief complaints were nausea, vomiting, headache, diarrhœa and severe abdominal pain. She was thirty-three weeks pregnant. The urine was essentially negative; the hæmoglobin was 57 per cent, and the white blood count was 15,500, with 80 per cent neutrophils. For ten days there was little change in her condition. Her temperature remained slightly above 99° except on December 16th, when it rose to 101.2. She was delivered of a premature infant on December 21st.

On December 22nd her temperature rose to 101° and remained elevated until January 5th. During the two weeks following delivery her general condition showed little improvement. Her diarrhœa persisted and on one occasion blood clots were passed in her fæces. On December 27th her hæmoglobin was 35 per cent, and her white blood cells 18,700, with 83 per cent neutrophils. Standard Kahn and Hinton tests were negative. A blood culture taken on December 28th showed no growth. From her lochia we cultured only *B. coli*, but from her fæces a heavy growth of *Pseudomonas aeruginosa* was isolated. Subsequent to January 5th she gradually improved, and was discharged on January 23rd.

The premature infant which was born on December 21st fed poorly from birth. On the fifth day large reddened areas appeared over the entire surface of the body. These disappeared on the sixth day, but the infant became markedly cyanosed and died.

Autopsy report.—The body was that of a six-day old Indian infant. External examination showed a large hæmangioma over the lower abdomen. Examination of the chest revealed a patent foramen ovale and congenital atelectasis of the left lung.

Examination of the brain was of particular interest. An area of hæmorrhage was present in the tentorium. In the sub-arachnoid space over the surface of the meninges, particularly basally, there was a considerable amount of material resembling coagulated serum. The ventricles were filled with a more purulent fluid. Smears taken from these locations showed a relatively small number of pus cells and many beaded, Gram-negative rods. On culture, pure growths of *Pseudomonas aeruginosa* were obtained. These proved virulent for mice, killing the animals in less than 18 hours when injected intra-peritoneally.

SUMMARY

1. A fatal case of meningitis of the new-born due to *Pseudomonas aeruginosa* is presented.

2. Birth was premature and birth injuries and congenital abnormalities were present.

3. At the time of labour the mother was suffering from severe diarrhœa. *Pseudomonas aeruginosa* was isolated from her fæces.

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Case Report

A CASE OF MULTIPLE ARTERIAL THROMBOSES OCCURRING IN A PROFESSIONAL BLOOD DONOR

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L.E., aged 44 years, an unemployed skilled mechanic and a professional blood donor, was admitted to the Montreal General Hospital, as a transfer from St. Luke's Hospital, March 30, 1938.

Complaints.—Weakness of the left arm and leg; difficulty in speaking.

The family and personal history were negative.

Present illness.—The patient had been a professional blood donor for three years. It is impossible to trace exactly how frequently he had given blood during this period. On March 4th he gave a transfusion of 375 c.c., and on March 9th, a second transfusion of 500 c.c. Immediately following this, he visited a tavern and ordered a glass of beer, and this is the last thing he remembers. Before he had time to take his drink he suddenly became unconscious, and was removed to St. Luke's Hospital.

When examined in hospital he was deeply unconscious, and showed a left hemiplegia with incontinence of urine and fæces. His blood pressure was 120/80. There was no evidence of peripheral arteriosclerosis, and examination of his heart did not reveal any murmurs. A lumbar puncture showed nothing abnormal.

He regained consciousness in three days, and it was found that he had a complete anæsthesia of his left arm and leg, and also was unable to speak. During his stay in St. Luke's Hospital his speech slowly returned, and he was able to move his left arm and leg. Seventeen days after admission he was able to move about the ward. At this time, it is reported that he showed a slight hypochromic type of anæmia and a mild leucocytosis. Also that his differential blood count showed no abnormalities. His urinalyses and blood chemistry were normal. His blood Wassermann test was negative.

Fifteen days after his cerebral accident he suddenly developed a severe knife-like pain in the left upper quadrant of the abdomen, which was aggravated by deep respirations. Examination showed a palpable, slightly tender spleen, and a leucocytosis of 9,000. This

pain lasted 24 hours, then recurred in four days. His urinalysis showed no evidence of red blood cells. There was no gross or microscopical blood in the stool.

At this stage, he was transferred to the Montreal General Hospital. Examination showed a moderately well-nourished man, looking older than the stated age, with a definite degree of pallor, and complaining of a pain in the left infracostal region on coughing or sneezing. His temperature was elevated to 100.60° F. There was slowing and slurring of the speech. It was typically syllabic and staccato, like that found with disseminated sclerosis. There was also impairment of memory with occasional mistakes in forming words. He could recognize and name any ordinary object. There was no difficulty in writing his name. His appearance suggested a hæmoglobin of 11 grams. The temporal vessels were not visible or palpable.

There was no evidence of infection in the upper respiratory tract. Examination of the chest revealed some dullness for a hand's breadth at the base of the left lung posteriorly, but the breath sounds were everywhere vesicular. There were a few fine moist inspiratory râles at the bases of both lungs. The lung dullness had disappeared by the following day.

The cardiovascular system seemed quite normal. The radial and brachial arteries were not thickened. The blood pressure was 110/60, R.C.D.

$$\frac{\text{III R}}{\text{2.5 cm./9 cm.}}$$

The sounds at the apex and base were clear, and the aortic second sound was not accentuated.

There was definite tenderness and resistance in the left upper quadrant of the abdomen but the spleen could not be palpated, nor was any enlargement recognized by percussion. The flanks were clear. There was no costo-lumbar tenderness, and the kidneys were not palpable.

An examination of the central nervous system by Dr. F. H. Mackay was reported as follows.

"Patient is now recovering from a severe left-sided hemiplegia with unconsciousness.

"He shows: (1) Staccato speech quite marked. (2) Lateral nystagmus to either side. (3) Spastic paresis of left face, arm and leg, most marked in left arm. The facial paresis is of the lower type. Tone is increased over left arm and leg. (4) Sensation at present is normal, though it was totally gone over the left side on admission. (5) The reflexes are as follows:

	Right	*Left*
Knee jerks	+++	++++
Ankle jerks	++	+++
Plantars	Flexion	Extension
Chaddock	Flexion	Extension
Oppenheim	Flexion	Extension
Abdominal, upper	++	++
Abdominal, lower	++	++
Radials	+++	+++
Biceps	+	++
Hoffman	0	+
Ankle clonus	0	+

"The pupils are equal, small, and react to light and accommodation. On examination of the fundi the discs are clear and the vessels are normal in outline. There is no exudate or hæmorrhage.

"The signs show left-sided hemiplegia, recovering (with, at first, left hemianæsthesia).

"The generalized motor and sensory involvement would suggest posterior capsular involvement.

"The nystagmus and speech defect would suggest cerebellar involvement, probably by implication of the superior peduncle. If so, this would be explained by a partial thrombosis of the left posterior cerebral artery."

Our impression on admission was as follows.

"The findings today point to a right cerebral lesion, and the history of onset is that of a hæmorrhage or embolus rather than a thrombosis. The speech difficulty strikes one as a dysarthria rather than a true aphasia. As regards the onset of pain and tenderness in the left upper quadrant, it certainly suggests a splenic infarct, but I am unable to state where the emboli are coming from."

A blood study showed: red blood cells, 4,260,000; white blood cells, 10,130; hgb., 9.5 grams, 67 per cent; polymorphonuclears, 68 per cent; lymphocytes, 28 per cent; eosinophiles, 2 per cent; monocytes, 2 per cent; platelets, 264,000; bleeding time, normal; coagulation time, 11 minutes (Lee and White); retraction of clot, normal; Hess test, negative.

A lumbar puncture gave an initial pressure of 165 mm. of H_2O with normal cardiac and respiratory oscillations. On jugular pressure there was a rapid rise to 360 mm. of H_2O with a quick return to 160 mm. H_2O on releasing the pressure.

The cerebrospinal fluid was clear. The Pandy test was negative, and only eight cells (mononuclears) per c.mm. The spinal fluid Wassermann and colloid gold tests were negative. Total protein, 0.037.

Urine analysis: specific gravity 1.020; albumin, none; glucose, none; microscopically, negative.

Blood chemistry: urea nitrogen, 14 mg. per 100 c.c.; creatinine, 1.62 mg. per 100 c.c.; sugar, 0.111 per cent; van den Bergh, 0.2 units.

Urine: urobilinogen present in 1/25 dilution.

Sputum examination was negative for acid-fast bacilli.

An x-ray of the chest showed no definite disease.

Four days after admission the patient was seen in consultation with Dr. A. H. Gordon, who made the following bedside note:

"The occurrence of the attack after giving two transfusions in rapid succession is noted, as is also his statement that the attack came on before taking any of the beer ordered.

"The chest film shows quite marked hilum thickening and some blurring at the left base.

"One cannot exclude metastases from a primary bronchial lesion, but the probability, to me, is cerebral thrombosis, and I feel that there has been some definite aphasia aside from anarthria, even though the cerebral lesion is right-sided."

During the eight days following his admission his temperature gradually returned to normal and the pain in the left upper quadrant of the abdomen had subsided. The left hemiparesis and his disturbed speech remained stationary.

Suddenly, on the morning of the ninth day in hospital, he asked for a bedpan, and about three minutes later complained of a severe pain all over the abdomen. His bowels did not move. When seen at this time by the resident there was no tenderness of the abdomen and nothing abnormal felt. His blood pressure had risen to 155/70; the pulse was 64 per minute; and the leucocyte count, 8,400. In an hour and a half, as the patient was still complaining bitterly of pain, he was given morphia, gr. ¼, hypodermically. Twenty minutes later the resident noted that there had been no relief of pain, that the pain was still confined to the abdomen, with no radiation to chest or down either arm. He suspected "a renal or some other colic", and injected morphia, gr. ¼, hypodermically. When examined by the attending physician, four hours after the onset of his abdominal pain, it was noted that the patient was still having very definite pain in spite of morphia, gr. $\overline{ss}$., that his colour had not changed, that he was afebrile, and his pulse 112 per minute. He preferred to lie on either side rather than on his back. When asked to localize his pain, he pointed to the upper abdomen, but moved his hand down around the umbilicus. He described his pain as steady in character.

The abdomen was normally rounded and moved freely with respirations. The lower half was soft, but the upper half somewhat resistant, with definite splinting in the epigastrium. No shifting dullness could be recognized in the flanks. There was no costo-lumbar tenderness, and no replacement of the normal area of liver dullness.

The note made at this time was as follows.

"From the steady character of the pain, its sudden onset, and the above findings on examination, I would suspect a perforated peptic ulcer. In view of the previous cerebral accident, and the suspected splenic infarction, the possibility of a mesenteric thrombosis must be considered. Surgical opinion to be requested."

He was seen immediately by Dr. Archibald Stewart, who also considered the condition to be one of either perforated peptic ulcer or a mesenteric thrombosis, more likely the latter, and advised operation.

This was done under gas oxygen anæsthesia, and when the abdomen was opened there was found to be a lack of pulsation in any of the vessels derived from the superior mesenteric artery, with a purplish-red discoloration of the intestines supplied by this artery. This discoloration became more marked during the course of the operation. It was also noted that there was a recent infarction of the spleen, which was adherent to the parietal peritoneum.

Owing to the patient's condition it was impossible to contemplate any further surgical interference, and the abdomen was closed. He died twelve hours later.

Autopsy.—Unfortunately permission was not granted to examine the brain, but otherwise a complete autopsy was done.

There was no gross evidence of arteriosclerosis of the peripheral vessels. There was some calcification in the abdominal portion of the aorta. In the superior mesenteric artery, 3.5 cm. from its origin, there was a pale pinkish-grey thrombus 1.8 cm. in length. It was lightly adherent to the arterial wall. Beyond this, along its branches, were dark moderately firm clots. The cœliac axis, the inferior mesenteric, and renal arteries were not involved.

The heart showed a slight degree of hypertrophy, but there was no evidence of endocarditis or mural thrombi. The orifices of the coronary arteries were quite widely patent and probed with moderate ease.

The lungs were congested, but no evidence of acid-fast infection or carcinoma was found.

On examination of the abdomen there was found to be a purplish red discoloration and œdema of all but the proximal two feet of the small bowel, the cæcum and the proximal foot of the colon. The involved portions of the intestines contained thin bloody material.

The spleen was large, 210 grams, and rather firm. There was evidence of a recent infarction of the middle third, and an adherent thrombus in the lumen of one of the arteries of the hilus. The splenic artery, along the upper border of the tail of the pancreas, was filled with a pale pinkish-grey thrombus.

Grossly, the marrow of the vertebræ and ribs appeared normal, but that from the upper third of the right femur was thick and purplish in colour.

Microscopic examination.—There was evidence of hypertrophy of the muscle fibres in the left ventricle. The left coronary artery showed no lesion except for several perivascular polymorphonuclear infiltrations in the adventitia. No lesion was found in the aorta, but it will be recalled that grossly there was evidence of some calcification in the abdominal portion. The section taken from the superior mesenteric artery contained a typical and fairly recent thrombus.

The spleen showed an area of necrotic infarction. The splenic artery, at the tail of the pancreas, was partially occluded by a typical thrombus. There was no sclerosis of the vessel wall, but the adventitia was infiltrated by polymorphonuclear leucocytes and eosinophiles.

The marrow from the right femur was definitely hyperplastic, the cells being both myeloid and erythropoietic. That from the ribs and the vertebræ was mildly hyperplastic, with a slight preponderance of erythropoietic elements.

The final *pathological diagnosis.*—(1) Superior mesenteric artery thrombosis; (2) hæmorrhagic ascites; (3) infarction of the small intestine in all but its proximal two feet; (4) infarction of the cæcum and part of the ascending colon; (5) splenic arterial thrombosis; (6) splenic infarction; (7) cardiac hypertrophy, slight; (8) mild arteriosclerosis; (9) hyperplasia of the bone marrow.

In summary, then, we have the history of a professional blood donor of some three years' standing becoming suddenly unconscious following the giving of two transfusions in rapid succession. He had developed a complete left hemiplegia with aphasia.

On physical examination no definite cause could be found for this cerebral accident. A hæmatological study by the ordinary methods gave no definite evidence of anything abnormal in the blood itself. His serological tests were normal. In rather rapid succession he went on to develop a splenic artery thrombosis, and a thrombosis of the superior mesenteric artery. These were confirmed by the autopsy, but no explanation for their occurrence was discovered.

All of which raises the question as to whether frequent transfusions bring about some abnormal changes in the hæmopoietic system which we are unable to discover by the methods at present at our disposal.

In conclusion, it would seem advisable to keep a very close check on all professional blood donors, and thereby limit the number of transfusions they may give within a specified time. In view of our present day knowledge, it would be interesting to speculate what this man might have shown as regards his prothrombin time.

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J. Gourevitch (*Thèse de Paris*, 1940, No. 192), who records 3 illustrative cases in men aged from 25 to 33, states that intoxication by manganese, first described by Cowper in 1837, though rare, is likely to become more frequent owing to its use in war industry. When fully developed it is characterized by a pseudo-Parkinsonian syndrome with the following features: disturbance of gait, change of facial expression, affection of the voice and speech, tremors, subjective sensory troubles, and psychical disorders. The course of the disease is chronic, even if the patient is removed from the toxic environment. Individual prophylaxis consists in washing the hands and cleaning the mouth after work and before meals. A special dress should be worn as well as a mask. Collective prophylaxis is effected by removal of manganese dust and vapour in the workshops and periodical examination of the workers to detect early cases of the intoxication.—*Brit. M. J.*, 1940, **2**: 499.

Editorial

INFLUENZA

WITH changing social conditions are associated changing medical conditions. In different periods different diseases have taken on a different emphasis. In Jenner's time smallpox was probably the most important of the communicable diseases. Vital statistics of his day were meagre, but there is good reason to believe that practically every city dweller then contracted smallpox. In fact the disease was so feared that large numbers of people voluntarily inoculated themselves in favourable seasons in order to escape natural infection in unfavourable seasons. With the growth of cities and the development of public water supplies typhoid fever waxed as smallpox waned, but typhoid fever in its turn yielded place to other diseases, and now if we survey the situation it is probable that influenza takes first place.

In terms of nuisance value the common cold stands very high among modern diseases, but we do not see the serious complications from colds which occur following influenza. The great pandemic of 1918, which visited nearly every corner of the world, is believed to have killed upwards of ten million people; in all the history of mankind no epidemic has equalled this one in intensity.

In 1918 it was assumed that the influenza bacillus was the cause of influenza, but this assumption was quickly found to be untenable. Fifteen years passed by before anything was discovered of importance regarding the cause of the disease. In 1933 Smith, Andrews and Laidlaw, in England, were able to inoculate ferrets with the throat washings from patients suffering from influenza. At the same time they demonstrated the development of antibodies against the virus in the blood of convalescents. Since this discovery other workers have confirmed the findings, and there now seems to be general acceptance of the view that influenza is a virus disease and that it can be identified by inoculation of ferrets and by certain immunological reactions. We have now a precise, though somewhat cumbersome, method of diagnosis and one which can differentiate several fevers which up till now have been loosely grouped together as influenza.

Stuart-Harris, Andrews and Smith and others[1] in England have given considerable thought to this differentiation, and they propose a classification of upper respiratory infections into various groups. The first group is epidemic influenza, which, practically speaking, is the disease which, on inoculation into ferrets produces a disease similar to that of man. The second group is febrile catarrh, difficult to distinguish from influenza clinically, but characterized by a more insidious onset and by more pronounced respiratory symptoms. The third group is simple coryza and pharyngitis—the common cold, and the fourth group is streptococcal tonsillitis. This is a useful classification, but it is by no means certain that epidemic influenza constitutes a homogeneous group, for epidemics of apparent influenza have been reported which do not produce disease in ferrets. Horsfall[2] and others at the International Health Division of the Rockefeller Foundation have proposed that influenza caused by any strain of the virus discovered by Smith, Andrews and Laidlaw be called Influenza A and that as other influenza viruses are discovered the diseases could be called Influenza B, C, D, etc. Since no strains are available from the 1918 epidemic we are in ignorance as to whether that epidemic was caused by Influenza A or some other unknown agent.

In the few years which have passed since the discovery of the Influenza A virus considerable laboratory work has been done and certain interesting findings have been recorded. It has been shown, for example, that an attack of the disease results in the

1. STUART-HARRIS, C. H., ANDREWS, C. H. AND SMITH, W., WITH CHALMERS, D. K. M., COWEN, E. G. H. AND HUGHES, D. L.: A study of epidemic influenza with special reference to the 1936-7 epidemic, Medical Research Council, Special Report Series, No. 228, His Majesty's Stationery Office, London (1938).

2. HORSFALL, F. L.: Present status of knowledge concerning influenza, *Am. J. Pub. Health*, 1940, **30**: 1302.

production of immune bodies which have protective qualities. There is a suggestion, too, that certain individuals develop antibodies without suffering from clinical disease, and one can speculate as to the rôle of these persons in the spread of the disease. Evidence has accumulated also to the effect that the immunity which is developed is comparatively short lived, probably not more than 6 to 12 months in duration.

Naturally, efforts have been made to develop a vaccine which will protect against the disease and a serum which will be effective in the treatment, but until recently these efforts have been disappointing. A few months ago Horsfall and Lennette[3] described a new vaccine which is unique among vaccines, and, on the basis of animal experimentation, promises much. Quite by accident, they discovered that ferrets which had been inoculated against ferret distemper with a vaccine prepared from ferrets inoculated both with influenza and distemper virus, became resistant to the inoculation of massive doses of human influenza virus. And not only were they resistant to one strain of virus but to several antigenically different strains. As a matter of fact, the immunity of the distemper influenza inoculated ferrets was substantially greater than that which resulted from actual infection with the influenza virus. Since this observation a vaccine has been produced by inoculating ferrets simultaneously with mixtures of human influenza virus and canine distemper virus. On human volunteers this vaccine has produced antibodies active against several strains of human influenza virus.

This latest discovery offers perhaps the greatest hope for a practical method of fighting influenza. Since the 1918 pandemic many epidemics of influenza have visited us. In terms of morbidity they have been astonishingly severe, involving at times probably a quarter of the population. In terms of mortality they have been exceedingly mild. An uneasy feeling always exists that the farther we get from the 1918 holocaust the nearer we get to the next one. So far our methods of control have not improved, but should these recent discoveries prove translatable into practical measures we might hope to see influenza join the ranks of smallpox and typhoid fever as a vanishing disease. Like aid to Britain time seems to be the essence of this problem.

FRANK G. PEDLEY.

3. HORSFALL, F. L. AND LENNETTE, E. H.: A complex vaccine effective against different strains of influenza virus, *Science*, 1940, **91**: 492.

Editorial Comments

Mortality and Morbidity from Alcohol

There is probably no factor whose influence in the production of disease is more difficult to define than that of alcohol. When one also considers the feeling that exists in many minds against alcohol in any form at all, together with the equally definite belief in its virtues in moderation, it is clear that inquiry into its disease-producing effects is peculiarly difficult.

Two recent papers illustrate this difficulty.[1] The first is a study of mortality from alcoholism in the United States. The writer points out that there are limitations to the available data on this point, not the least of which is the unwillingness of some physicians to certify to alcoholism as a cause of death. However, even if the data are of no great value as absolute measures, they are reliable in comparing the relative incidence of mortality from alcoholism in various areas and groups.

For the year 1938 acute and chronic alcoholism were certified as the primary cause of death in 2,569 cases, representing 20 per 100,000 of the population. The general trend of mortality from alcoholism throughout the country during the period 1900-1938 is downward, declining from 6.0 per 100,000 in 1900 to the 2.0 per 100,000 already noted. The highest rate was reached in 1907, and the lowest coincided with the early years of the prohibition period, but the subsequent rise never reached pre-prohibition heights, and in recent years the figures have notably declined.

The geographical distribution of this mortality is shown to be extremely difficult of analysis because of the many factors involved. The charting of deaths due to alcoholism shows that the State of Nevada has a rate of 12.5 per 100,000 of population, more than double that of the next highest rate of 5.6 in Delaware, whilst such densely populated and urbanized states as New York, Massachusetts, Pennsylvania and other Eastern States, have rates varying between 3.0 to 3.9. Obviously, the high rate in Nevada must be due in part to the large num-

1. SCHMID, C. F.: Mortality from alcoholism in the United States.

ber of non-resident deaths as compared with the population of the State. The same phenomenon occurs in certain States with respect to the mortality from tuberculosis.

The second paper[2] deals with the age-long question of the association between alcoholism and cirrhosis of the liver. It is based on the study of 210 cases of cirrhosis seen at autopsy in the Philadelphia General Hospital, for the two years 1938 and 1939. In spite of our lack of definite knowledge as to the cause of cirrhosis, as well as contradictory experimental evidence, there is still a persistent tendency to associate atrophic (Laennec's) cirrhosis of the liver with chronic alcoholism, although the same type of cirrhosis may be demonstrated in children and others with no alcoholic history, and, in addition, many confirmed alcoholics do not develop cirrhosis.

The results of the present study show that there was an alcoholic history in only 32.4 per cent of all types of cirrhosis, and in 45.5 per cent of portal cirrhosis, usually called "alcoholic". Cirrhosis occurred about ten years earlier in those with alcoholic history than in the non-alcoholic, and more frequently in the male than in the female. It was concluded that alcohol might play a rôle in an undetermined number of cases of cirrhosis, but it is also to be realized that factors other than alcohol must be responsible. "Portal cirrhosis" and "alcoholic cirrhosis" therefore should not be used as synonymous terms. H.E.M.

2. BOLES, R. S. AND CREW, R. S.: Observations on chronic alcoholism and cirrhosis of the liver, *Quart. J. of Studies on Alcohol*, 1940, **1**: 432 & 463.

Financing the War

We have been passing through another stage of impassioned appeal for the contribution of funds to prosecute the war and, no doubt, others will follow. The issue is again brought up to us. What are we going to do about it? We are so comfortably and so safely placed in Canada that it is hard to realize the grievous plight of our kinsfolk in the Mother Land and the urgency of their situation—a situation which may become ours, for all we know. We believe that this consciousness is at long last being borne in upon us. What are we going to do about it? We are told that "Faith is the substance of things hoped for". We believe that we shall win the war, but certainty and complacency will not do it; we must translate tenuous faith into substantial result. We can do it, for there is plenty of money still in Canada despite the drain of one year and a half of war. Sir Henry Drayton, in an address given not long since before a meeting of a War Savings Committee in Toronto, said this:

"This country has the money to meet the goal set for the February pledge campaign," he said. "I have figures of October 31, 1939, before the earning power was swollen by war industries. On that date, deposits amounted to more than a billion dollars and accounts of $1,000 or less represented 92 per cent of the whole. Accounts of $1,000 to $5,000 represented 7 per cent. So together these two modest classes represented one billion dollars.

"So you can see that if this was the case in October, 1939, there is any amount of untapped money in the hands of the Canadian people of small means waiting for you to glean.

"There's not a family, speaking generally, which is not in an infinitely better position than it was a year ago. The number of men employed in Canada has gone up tremendously. And this is in great degree because England is spending her money in Canada. Because England has thrown the securities of her people on the bargain table so there'll be money to pay for this war, which is just as much ours as hers. Can any Canadian decline to return to the common defence every single cent of money the mother country has been spending here?"

The healthy state of our finances here in Canada is set forth in detail by a bulletin issued in February, 1941, by the Royal Bank of Canada. The following excerpt is worth noting:

"Barometers of business activity practically all recorded expansion during the year, the official index of the physical volume of business being 19 per cent higher in 1940 than in the preceding year and 15 per cent higher than in 1929. The following table is a comparison of the principal official indexes for the first eleven months of 1940 with the corresponding months of 1939 and 1938.

INDEXES OF CANADIAN BUSINESS

(1926 = 100)

	First eleven months		
	1940	1939	1938
Physical Volume of Business	144.7	121.4	112.7
Industrial Production	152.7	124.5	114.3
Manufacturing	145.8	117.3	107.1
Mineral Production	239.2	215.4	195.7
Employment			
General Index	124.2	113.9	111.8
Manufacturing	131.3	112.3	111.2
Logging	166.9	119.1	142.8
Mining	168.4	163.8	155.9
Construction	90.7	113.0	105.4
Building	83.5	62.2	60.1
Highway	122.1	218.8	198.1
Trade	142.9	136.6	132.6
Wholesale Prices	82.8	74.9	79.1
Cost of Living—November*	107.8	103.8	102.2†

* 1935-1939 = 100.
† Average for year."

No doubt, then, of our ability to pay.

How much do we need, in round figures? We quote from Bulletin No. 2 issued by the Canadian Publishers War Finance Publicity Committee.

"It is, of course, impossible to forecast what Canada will spend on war in the next fiscal year. The cost is bound, as the war intensifies and as we pass from defensive to offensive, to be much greater than now. That is about as far into the future as we can speculate. But of the current fiscal year it is quite possible to picture the approximate situation and illustrate the need of the current fiscal year in a very few trenchant figures, as follows:

	Millions
Canada's Probable War Expenditures ....—say	$ 850
Cost of non-war Government activities (Hansard, June 24, 1940, page 1120)	450
	$1,300
Less Revenue (Estimate based on current tax yields) .....—say	780
Approximate deficit for the fiscal year	$ 520

"It is true that the Dominion began the fiscal year with a large amount of available cash ($187 millions), but it is obvious that to conduct its operations on the enormous scale of the present large amounts of cash are required at all times. If we assume that cash available at the beginning of the year might be reduced by, say, $137 millions, this would leave $383 millions of the deficit to be financed.

"To this sum must be added a very large and almost unpredictable amount in financial aid to Great Britain. (Canada has undertaken, in addition to all her own war expenditures, to give all the help she can to the United Kingdom by making as many Canadian dollars available to her as possible for Britain to use in her own war purchases here. This is done by repatriating Canadian securities. In the June budget a sum of $200 million was assumed, but the actual amount required will probably be much larger.) If we assume $300 million and add it to the $383 million given above, it is seen that, without looking into next year at all, Canada needed to, or needs to raise by war savings certificates and by war loans during the present fiscal year, probably not any less than $683 million."

This forecast is rather appalling, but we must face it.

In view of the possibility that the war will be a long one, and feeling that our financial resources should not be exhausted prematurely we must do some planning. Some of this planning is being done for us—witness the greatly increased taxation schedule—but the tooth-drawing was made somewhat less painful by the provision that we could pay our dues in instalments. Other planning is left to ourselves—we can buy Savings Stamps, War Savings Certificates, and War Bonds. If we are wealthy we can lend the Country money without interest or give money as a gift. Those who are not so wealthy can link up with the many patriotic and philanthropic agencies. What form our efforts take will necessarily be guided by our financial situation and our future requirements. There are a sufficient number of plans to enable us to make a wise choice. Only, let us make some choice. The need is great and immediate. A.G.N.

Bis dat qui cito dat.

Special Article

THE TUBERCULOSIS PROBLEM IN CANADA*

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It is proposed in this paper to give an outline of the tuberculosis problem in Canada. An attempt will also be made to indicate the extent to which the campaign against the disease has developed and the avenues which should be further explored to increase its efficiency.

The problem varies according to the different provinces of Canada, and more particularly according to the four geographical divisions of the Dominion, as the following table and the remarks will indicate.

TABLE I.

TUBERCULOSIS DEATHS AND DEATH RATES FOR CANADA 1937, 1938 AND 1939[1]

	Total No. of deaths			*Death rates*		
	1937	*1938*	*1939*	*1937*	*1938*	*1939*
Canada	6650	6122	5972	59.9	54.7	52.8
Prince Edward Island	65	81	62	69.9	86.2	65.3
Nova Scotia	457	412	428	84.3	75.2	77.3
New Brunswick	383	341	286	87.0	76.6	63.4
Quebec	2769	2616	2680	88.3	82.5	83.5
Ontario	1315	1237	1084	35.4	33.2	28.9
Manitoba	426	349	367	59.4	48.5	50.5
Saskatchewan	296	271	233	31.5	28.8	24.6
Alberta	339	280	282	43.6	35.8	35.7
British Columbia	600	535	550	79.9	70.3	71.1

Analyzing the statistics for 1937-38-39, we find a reduction from 6,650 deaths to 5,972, and a fall in death rate from 59.9 to 52.8 per 100,000. Over the three years there is a substantial reduction in every province showing either in 1938 or in 1939. Wherever an increase occurs it is slight and offset by a greater reduction in the other years. This is quite striking in the Maritime Provinces, also in Manitoba, Alberta and British Columbia. Ontario and Saskatchewan have registered new low rates for 1939, and are now under 30, their rates being 29.5 and 24.6 per 100,000, respectively. When treaty Indians are excluded, the rates for these provinces are 26.1 and 17 per 100,000. The Indian deaths in Canada amounted to 11 per cent of the total, although the Indians comprise only 1 per cent of the population. When the Indian deaths are excluded the rate for Canada is reduced from 52.8 to 47 per 100,000.

When we examine provincial death rates we see the following rather striking comparisons. The rate for Ontario and the Prairies is about 34 per 100,000. The rate for Quebec and the Maritime Provinces is about 80 per 100,000. Ontario and the Prairies have 55.7 per cent of the population; they contribute 34.9 per cent of the deaths. Quebec and the Maritimes are 37.4 per cent of the population; they contribute 56.2 per cent of the deaths.

Are there any special reasons for these variations in the tuberculosis death rate in Canada? We know that treatment facilities in Ontario and the Prairies are double those of Quebec and the Maritimes. In our enthusiasm we are apt to conclude that this is the only reason. While

* Read at the Fortieth Annual Meeting of the Canadian Tuberculosis Association, Montreal, June 27, 1940.

we believe that these facilities are playing a great part in the campaign, we must remember that Quebec and the Maritimes are making just as great an effort, but their problem is more than twice as great, and they require twice the facilities according to their population.

These provinces always had a very high death rate compared with the others. A factor which has been always mentioned is the difference in age of the population. If the rate is standardized for age, it increases the rate for the Prairie Provinces and lowers the rate for the Maritimes. But this still leaves them with very different rates, and as the population of the Western Provinces ages this factor is of less significance.

Then, there is the economic factor. We know that tuberculosis will vary according to the average of wealth of a community. This would seem to throw some light on the situation. The Commission on Dominion-Provincial Relations has shown us that the Maritime Provinces have 9.7 per cent of the population. They have only 6.4 per cent of the wealth, but they have 13.5 per cent of tuberculosis deaths. Quebec has 27.7 per cent of the population, 26.1 per cent of the wealth, and 42.7 per cent of the deaths. Wealth is concentrated in certain centres so that it is possible that the average in a great part of the province is below the provincial average.

Race has an influence on death rates in Canada. While we have not the negro population of the United States, Nova Scotia has 7,361 listed as coloured, which is one-third of the negro population of Canada. We have the Indian problem, particularly in Ontario and the four Western Provinces. British Columbia is particularly affected by racial factors, having an Indian problem and also an Oriental problem. The white rate is around 45 for British Columbia, but Indians and Orientals increase the rate to 71.1 per 100,000.

Dr. Eugene Gagnon[2] has made a very excellent study of tuberculosis of the Jewish race in Montreal. A study of the mortality from tuberculosis according to other nationality groups gives some interesting figures. The French-Canadian rate was 95.8; the English-Canadian rate was 57.0; the Jewish-Canadian rate was 26.6. It was also pointed out that the proportion of beds per death varied as follows. For the French-Canadians there was 0.9 per death, for the English-Canadians 3.8 per death, and for the Jewish group 6.6 per death. It should be noted, however, that every institution treats all nationalities.

Whatever factors there may be to account for the great variation in death rates in Canada, there is no doubt as to the great reduction that has taken place—a rate of 52.8 per 100,000 as compared with approximately 200 per 100,000 in 1900. It is even more, as the 1900 rate did not include Indians.

For years, epidemiologists such as Greenwood[3] have sought to explain the fall in death rate on grounds other than the active campaign against the disease. The three arguments commonly used are: (1) That tuberculosis, like other communicable diseases, runs in cycles, but that its cycle is a large one, taking one hundred years to be completed. The prediction was made that after 1915 the disease would increase. It is enough to say that the greatest reduction has taken place since that time. (2) That we are developing an increased resistance to the tubercle bacillus. While this is evidently true to a limited extent, as is the case with primitive people, there is evidence that although people such as the Chinese have been exposed to massive tuberculous infection for centuries, tuberculosis is still a major disease. (3) Improved standards of living. This is probably a factor of greater importance than the other two, when we consider the great advances that have been made in the matter of diet, and probably it would exert a greater effect if these benefits could be distributed to a greater proportion of the population.

The greatest reduction in tuberculosis has taken place coincident with the campaign for an organized system of control against tuberculosis, based on the early diagnosis of the disease and the segregation and treatment of all active cases, so that we are forced to conclude that this is the factor of greatest importance. The decline in tuberculosis is in proportion to the extent to which facilities for its cure and prevention have been developed. There seems to be a definite relationship between the number of sanatorium beds available and the decline in death rate. The two provinces that have death rates in the twenties (Ontario and Saskatchewan) have as many as three beds per annual death, and for the white population the rate has declined faster than in the other provinces. This decline over an eleven-year period was 38.3 per cent and 41.2 per cent, as compared with 27 per cent for the rest of Canada.[4] This calculation was made by the Vital Statistics Branch of the Dominion Bureau of Statistics by comparing the average tuberculosis mortality rates by provinces for 1922-25 and 1933-36. It was computed on the basis of exclusion of Indian and halfbreed deaths because their registration was incomplete in the four-year period from 1922-25.

While it is not possible to make an accurate comparison of the white rate for 1921 and 1939, as it is difficult to obtain an exclusive white rate for 1921, it is possible to make one which is sufficiently reliable to show a fair comparison. The official figures for tuberculosis deaths for 1921 contained very few Indian deaths and were, for practical purposes, a fair estimate of the white deaths of that year. We have used these to compare with the rates for 1939, after excluding the Indian deaths. These show

some very striking figures for the reduction over eighteen years.

TABLE II.

DECLINE IN TUBERCULOSIS DEATH RATES FROM 1921 TO 1939 IN WHITE POPULATION

	1921	*1939*	*Reduction percentage*
Canada	87.6	47	45.0
Prince Edward Island	144	61	57.0
Nova Scotia	134	77	42.0
New Brunswick	106	62	41.0
Quebec	122	81	33.0
Ontario	71	26	60.0
Manitoba	69	32	53.0
Saskatchewan	43	17	60.0
Alberta	53	19	64.0
British Columbia	78	46	41.0

The scientific basis for a program for the control of tuberculosis was well set forth by Frost.[5] He pointed out that, "For the eventual eradication of the tubercle bacillus it is not necessary that transmission (of the tubercle bacillus) be immediately and completely prevented." That, "It is only necessary that the rate of transmission be held permanently below the level at which a given number of infection-spreading (*i.e.*, open) cases can succeed in establishing an equivalent number to carry on the succession". In other words, can we isolate enough patients so that there will be a reduction in each year's crop of infection-spreading individuals?

The significance of this conception is, as pointed out by Godfrey[6] that if there is no change in the susceptibility of the tubercle bacillus, and if we increase our efforts in early diagnosis, adequate treatment and after-care, tuberculosis in the white race in this country and in the United States will in fifty years be about 5 per 100,000. If this is a correct outline of the situation, and I think many of us will agree with this conception, how are we to accelerate the decline?

The first requisite is to increase our sanatorium beds where these are needed. We have in Canada 10,088 beds for the treatment of tuberculosis. We had in 1939, 5,972 deaths from tuberculosis. The beds are distributed by provinces as follows:—

TABLE III.

	Beds	*Deaths*
Canada	10,088	5,972
Prince Edward Island	80	62
Nova Scotia	628	428
New Brunswick	525	286
Quebec	2,644	2,680
Ontario	3,624	1,084
Manitoba	762	367
Saskatchewan	768	233
Alberta	399	282
British Columbia	658	550

There are approximately 500 additional beds under construction, 300 at Sherbrooke, P.Q., 150 Indian beds in British Columbia, and other arrangements in Nova Scotia and Ontario will complete the five hundred under construction. This will make a total of 10,588 beds, or about 1,500 beds short of two per annual death. It will be seen, however, that while in Ontario and Saskatchewan there are three beds per annual death, Quebec and the Maritimes are far short of this quota. Beds for Indians are needed in Alberta and British Columbia. With an adequate number of beds it is possible to segregate enough open cases so that the rate of transmission can be kept continually below the level at which a given number of infection-spreading cases can be successful in infecting an equivalent number to carry on the succession.

There are other factors which may militate against the full use of sanatorium beds even when these are available. These we can influence to make the campaign as effective as possible.

We have by no means exhausted the possibilities of earlier diagnosis. It is true that we have made great headway in that direction. We have developed a very extensive system of tuberculosis clinics all across Canada, with an ever increasing number of cases examined and re-examined each year. We now examine all those cases referred by the general practitioners. This is the most fruitful source of new active cases. As they have consulted a doctor because of symptoms they are likely to be found advanced. Many of them will have positive sputum. They are a very important group.

In this connection I think it is worth while emphasizing the suggestion put forward by Godfrey,[6] of the New York State Department of Health, that the campaign for early diagnosis has been wrongly interpreted as meaning the diagnosis of early cases rather than the early diagnosis of all existing cases. The early diagnosis of a late case that is spreading tubercle bacilli under the guise of asthma or chronic bronchitis is just as important as treating an early case which is non-infectious. The co-operation of the medical profession in ferreting out these infectious cases is of greater importance than ever.

Then, there is the matter of the examination of contacts. They are second only to the group referred to tuberculosis clinics because of symptoms as a fruitful source of new discoveries. While a good job is being done in the periodic examination of contacts there is still a great deal more to be done. It seems to be easy enough to examine the contacts of known cases under fifteen years of age, but the group over fifteen are more important and are the ones that have hitherto been missed. We are not so likely to miss the original source of infection if all ages are examined.

We are only just beginning to appreciate the value of industrial surveys as a case-finding procedure, and it is our duty to extend these as widely as possible. So far the mining industry seems to be the only one that is being fairly well covered in Canada. In this case the companies themselves have been mainly responsible for its adoption because of their experience in the cost of compensation. Opportunities are legion for fostering the regular examination of groups of young and older adults.

It has been definitely shown that the incidence of tuberculosis in nurses and nurses-in-training is much higher than in the average population. In 1937[7] there were admitted to institutions in Canada, exclusive of British Columbia, 7,686 patients; this represented persons gainfully occupied. For nurses-in-training the rate was 6.8 and for graduate nurses the rate was 7.6; for practical nurses, midwives, hospital aides and orderlies the rate was 7.02. These rates are more than ten times the average for the rest of the population and exceed all other groups, the next being that of hard-rock mining where the rate was 3.9 or a rate of approximately six times the average. We are obviously dealing with groups that show the value of periodic examination.

The high incidence of tuberculosis in nurses and hospital employees has served to indicate that there is a great deal of hidden infection in the wards of general hospitals. Probationers who do not react to tuberculin on entering hospital rapidly receive their primary infection, as indicated by subsequent tuberculin tests. We must do a great deal more to identify these cases of tuberculosis that find their way into general hospitals with other diagnoses. Sputum examinations should be a routine order, as is urinalysis.

Tuberculosis is always a problem in mental hospitals, being the largest single cause of death in these institutions. Many open cases were to be found in the wards in close association with other patients. In recent years mental hospital authorities have made every effort to have these open cases recognized and segregated. Routine surveys have been carried out for this purpose, and the results of this policy have been justified in the reduction in tuberculosis deaths in these institutions.

The routine examination of normal school students and university students has developed in a very satisfactory manner. This has served to foster the idea that anyone who has to do with the care and supervision of children should be certified as free from tuberculosis.

Surveys of school children, both public and high school pupils, tend to increase perhaps beyond the wishes of many tuberculosis workers. Some even go so far as to say that these surveys should be discouraged because of the few active cases of tuberculosis found. While it is true that the incidence of tuberculosis is extremely low under fifteen, I know of no other procedure that has had a greater educational value in the community, and while it may be necessary to keep such surveys at a minimum, depending on the time and money available, it is a mistake to condemn them as has been done by a few health officials and tuberculosis officers. Such action tends to confuse the public, and shows a lack of appreciation of the necessity of educating the public to the need for constant vigilance in the search for hidden cases of tuberculosis.

The use of the tuberculin test has simplified surveys and saved a good deal of time and money in connection with them. Whether we should use O.T., P.P.D., or patch tests will remain the opinion of the individual carrying out the work. I can see no evidence of standardization, or the advisability of advocating any one test to the exclusion of others at the present time. The use of the miniature x-ray film would appear to be a great advance and a means of saving a great deal of money in our case-finding campaign.

In certain parts of Canada our treatment facilities are not being used to the full advantage, because the last barriers have not been removed in providing the cost of treatment so that a patient may be admitted promptly when a diagnosis is made. This has ceased to be a problem in the majority of the provinces and a patient can be admitted if necessary within twenty-four hours of the time when a diagnosis is made. Wherever it is still necessary to secure permission from the local county council before treatment can be authorized there is still delay and needless loss of time and unnecessary exposure by open cases.

A word should also be said about the standard of treatment given by our institutions. Can we say that the number of patients who leave against advice will give a clue as to whether the institution is giving all in its power to convince the patient of the necessity of treatment, or to give that patient all the treatment and attention necessary so that the stay will be as long as necessary, and the public afforded that protection from the open case that it has a right to demand? Certain it is that there is a great variation in the percentage of patients who leave against advice, the proportion varying from 6 to 28 per cent for the Dominion as a whole.[7]

What about collapse therapy and all the surgical aids which are now available? In spite of all the attention paid to collapse therapy and the use of pneumothorax, phrenic operations, intrapleural and extrapleural pneumolysis, paraffin packs, Monaldi operations, and even lobectomies for tuberculosis, I am still of the opinion that, by and large, collapse therapy is not overdone. In most instances the proportion is too low, and, with all the warnings

that are now being given, it is likely that the radical measures of today will be the conservative ones of tomorrow. Pneumothorax, intrapleural pneumolysis and thoracoplasty are measures that have stood the test of time, while we have still to evaluate the use of other methods. I think we are not yet clear on whether we give too much pneumothorax to minimal cases, whether we carry on pneumothorax too long (at least in those cases not receiving an effective collapse), and whether we are withholding thoracoplasty when it should be undertaken earlier. I can see no reason why pneumothorax should be given to only 25 per cent of the patients in one institution and to 60 per cent in another institution; or why thoracoplasty should be used in less than 1 per cent of discharged patients in one institution and in 10 per cent of discharged patients in another.

There has been a continuous cry for economy ever since the depression in the operation of tuberculosis institutions. We must be careful to see that operating costs do not fall below a minimum in which modern and effective treatment can be given. In many instances there is a great difference in the services rendered. While some give little more than a bed and custodial care, others give a complete surgical service, others carry on all the clinic and follow-up service in their districts. This must all be taken into consideration in assessing their value. There are a fair number of institutions operating on less than $2.00 a day. It is difficult to conceive how an institution can carry out the services necessary at less than this figure, and one feels that they are losing many opportunities and perhaps money invested in treatment if this is ineffective.

Then there is the after-care of the discharged tuberculous patient. The job of the institution is not completed when the patient goes home. The local physician, health officer, public health nurse, and the social worker (if such a department exists) will do their part in carrying out this important phase of the problem. One has only to consider the proportion of re-admissions that go to make up the sanatorium population to realize what an important phase of the work this is, and how easy it might be to undo and nullify the beneficial effects of treatment given and money expended if the discharged patient is lost from direct contact with either the sanatorium, the health department, or the private physician.

The responsibilities of the full-time tuberculosis officer, be he in the sanatorium or clinic, are great. He is responsible for efficient sanatorium treatment, which, with the increase in surgery, has greatly enlarged, but he must also interest himself in a field as wide as the ramifications of tuberculosis. He is responsible for the supervision of the patient from the time the diagnosis is made until the patient recovers or dies. His case-finding responsibilities and his interest in follow-up and after-care should make him as interested in the field as in the institution,—responsibilities which he must share with the private physician, public health department, and social service department. He must also take some responsibility for the continuous program of education of medical students and nurses, and of the population generally, whose interest and support is necessary if adequate funds are to be supplied to provide facilities so necessary if the campaign is to be entirely successful.

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Association Notes

Canadian Medical Association Convention
Winnipeg, June, 1941

PROPOSED SOCIAL PROGRAM

Medical Visitors—

Tuesday, June 24th.—Evening—Dinner at the Medical Council, the Winnipeg Medical Society being hosts.

Wednesday, Thursday and Friday—June 25th, 26th and 27th.

Luncheon at the Royal Alexandra Hotel addressed by outstanding visitors.

Evening—Ceremonial and Installation of the President of the Canadian Medical Association at the Royal Alexandra Hotel.

Association Reception and Dance at the Royal Alexandra Hotel.

Thursday, June 26th. — Evening — Alumni Reunion Dinner. Program, non-scientific.

Friday, June 27th.—Afternoon—Garden Party at Government House.

LADIES' PROGRAM

Monday, June 23rd. — Afternoon — Tea at the University Women's Club for the wives of members of the General Council.

Tuesday, June 24th.—Afternoon—Luncheon at the St. Charles Country Club for the wives of members of the General Council.

Tuesday, June 24th—*Continued.*

Evening — Supper (informal) at the Manitoba Club for the wives and members of the General Council.

Wednesday, June 25th—Afternoon—Reception at the St. Charles Country Club for members of the Association and their wives.

Evening—Ceremonial and Installation of the President of the Canadian Medical Association at the Royal Alexandra Hotel.

Association Reception and Dance at the Royal Alexandra Hotel.

Thursday, June 26th. — Morning — Breakfast Party at the Motor Country Club, Lower Fort Garry.

Evening—The Ladies Committee is arranging that the out-of-town wives be guests at dinner at the Fort Garry Hotel.

Friday, June 27th—Afternoon—Garden Party at Government House.

A Matter of Simple Arithmetic

INCOME TAX

There are still many doctors in Canada who ask the question, Why should I belong to the Canadian Medical Association? Many have not pursued this question to the point of providing themselves with answers which would prompt them to become members of the Association.

A subject, perhaps not a pleasant one, but one which is engaging the attention of most members of the medical profession at this time, is Income Tax. Several years ago, the Canadian Medical Association in co-operation with the Department of Income Tax for Canada produced a memorandum to guide the medical profession in the completion of income tax returns. It was the duty and privilege of the Canadian Medical Association to make every endeavour to have all legitimate exemptions to which the profession were entitled admitted as expenses. While the memorandum of eight years ago has been modified, having regard to the country's need of increased funds, the most recent announcement by the Federal Income Tax Department on the subject still takes cognizance of many expenses entailed in the practice of medicine. For example:

- A physician is allowed up to $100 exemption for fees paid to governing bodies and medical associations;
- The complete write-off of medical books purchased within the year of purchase;
- The complete write-off within the year of purchase, of instruments costing $50.00 or under;
- A very reasonable yearly write-off of instruments costing more than $50.00.

If these four items alone are taken into account as concessions which were granted the medical profession by the Income Tax authorities and a reasonable amount of credit be given the Canadian Medical Association for having secured such concessions, it will be found that a doctor who is obliged to pay any income tax has been saved more dollars than the cost of membership fees in his local, provincial and national medical associations.

What do I get out of the Canadian Medical Association? When figuring out *your* income tax this year, note the items referred to herein and calculate what the saving has been to *you*. A little simple arithmetic should prompt many a doctor in Canada who is not now supporting his medical organizations to hasten to remedy that omission on his part.

The annual fee of the Canadian Medical Association is $8.00 and is collected by all the provincial medical associations from those who, in the opinion of the Provincial body, are qualified and who want to be members. When you are invited by your provincial association to pay this fee along with that levied by the province, please remember that it is the cheapest and most valuable insurance you can buy. It should be a matter of simple arithmetic for you to determine that the Associations are protecting your livelihood.

Hospital Service Department Notes

Report of the Canadian Intern Board for Year 1940-41

Following the sound principles laid down last year by Dr. William Kerr in conjunction with the Canadian Medical Association and the Canadian Hospital Council, the Canadian Intern Board has completed a very successful second year. Like all new ideas, however, this plan has had to be tried and tested in every possible manner before its true value could be correctly estimated. We have been quite satisfied with the final results, since the Board has been put through practically every "acid test" in its early infancy, and still has every indication of becoming a robust child. However, in presenting this report, we want you to be the judges, and any criticism or suggestions for the future will be most welcome. This year a few necessary changes were made. One very satisfactory plan devised this year was that whereby the Board submitted to all the hospitals a list of students who were applying through us. This did away with the confusion encountered last year when a few hospitals

All communications intended for the Department of Hospital Service of the Canadian Medical Association should be addressed to Dr. Harvey Agnew, 184 College Street, Toronto.

placed the names of students on their hospital forms who had not submitted an application to the Canadian Intern Board.

The number of students applying through the Board has almost doubled this year. The following is a summary of the various universities: University of Alberta, 36 forms; Queen's University, 26 forms; University of Toronto, 115 forms; University of Western Ontario, 23 forms; Dalhousie University, 1 form; McGill University, 1 form; Yale University, 1 form. Total, 203.

We were particularly gratified by the very fine registration and by the enthusiasm shown by the University of Alberta students.

One hospital remarked that until every student applied the Board could not operate satisfactorily. For this reason we canvassed the schools to try and determine why we had not received an application from every final year student. The following reasons were given.

1. A certain number of students did not apply to Canadian hospitals, and consequently they would not benefit by submitting a form to the Canadian Intern Board.

2. A certain number of students at one school applied to a local teaching hospital which did not deem it advisable to submit a list to us this year due to local circumstances. However, these students did not apply to any other hospitals, so that this did not hinder the functioning of the Board. May we add that this hospital in question has voiced its approval of the Canadian Intern Board and hopes to enter under the scheme when possible.

3. A handful of students at one school was misguided into believing that they had a better chance of obtaining their appointments independently of the Canadian Intern Board at a certain hospital. However, this proved erroneous, since we received the fullest co-operation from that particular hospital.

4. At Dalhousie, Laval, University of Montreal, and the University of Manitoba the final year students serve their junior rotating internships during their last year at school. Since these appointments are aranged at these centres by selected hospitals and the medical schools concerned, the appointment problem is distinctly a local one. A somewhat similar arrangement exists at McGill.

It may be concluded, therefore, that all eligible students across Canada, with the very rare exception, applied for their internships through the Canadian Intern Board. The various representatives at each school have informed us that the plan was very satisfactory this year, as judged from student opinion.

Number of applications received from students .	203
Number of applications filled by Canadian Intern Board	188
Number of applications not filled (Alberta 2, Queen's 2, Toronto 10, Western 1)	15

Therefore the Canadian Intern Board placed 93 per cent of its applicants. At the present time there are only four of the original fifteen who have still not been placed. We believe that, by furnishing each of the above fifteen students with a list of hospitals that did not receive their full quota, and by furnishing the latter with a list of unplaced students, the Canadian Intern Board has made the above possible to a large extent. Also this year we have found that the number of broken contracts and "jumping" from one hospital to another has decreased considerably. We have heard of a few unavoidable instances where a student, due to financial or other reasons, was unable to accept his appointment, but in most instances we were able to have him arrange for a satisfactory substitute to take his place from among those not placed. In cases where a substitute was not available we did not encourage the move.

The following is a summary of how the students fared in their choice of hospitals.

University	*Hospital of 1st choice*	*2nd*	*3rd*	*4th*	*5th*	*6th*	*Total*
Alberta....	30	2	2	0	0	0	34
Queen's...	18	4	1	0	0	1	24
Toronto...	79	11	10	2	3	0	105
Western...	21	1	0	0	0	0	22
Others....	3	0	0	0	0	0	3
Total.....	151 (80%)	18 (10%)	13 (7%)	4, toge	5 an ther(	d 6 3%)	188 (100%)

Occasionally we have heard a student remark that he considered the Canadian Intern Board unnecessary and that he should be able to receive an appointment by means of the old system just as easily.

However, from the above figures and from the data we have at hand we can definitely state that the 80 per cent who were appointed to their first choice hospital would not all have fared so under the old system. In fact we can practically state that instead of 80 per cent it would have been approximately 55 per cent at the most. It is possible that the Canadian Intern Board does not play as important a rôle for the honour students, since they would have no trouble in obtaining their appointments, but for the remainder who make up the great majority there is no doubt now that they were benefited.

The only criticism received with regards to the students' part this year was that in a half a dozen cases they failed to apply *personally* to *all* the hospitals they had listed on their forms to us. However, where this was discovered it was rectified in every case.

Let us now consider how the hospitals fared. We received lists from 33 hospitals approved for internship. Hospitals in centres like Montreal, Winnipeg, etc., did not hand in lists, since they

obtain their interns from McGill and the University of Manitoba, etc., respectively.

One interesting fact noted was that the sum total of interns requested by the above thirty-three hospitals was two hundred and forty-six. Since there were only two hundred and three students applying through the Canadian Intern Board, it can be seen that it would have been impossible for us to fill every hospital's quota of interns.

Number of hospitals with quota filled	13
Number of hospitals with quota not filled	20

Of the twenty hospitals who did not receive their full quota, many were short one or two men, and we understand that they will be able to rectify their loss by obtaining men from the United States, final year students, and from students not placed as yet. Some have already filled their quota by means of the list sent them of unplaced students.

There were, however, five or six hospitals that were left "out in the cold." Of this number we were unable to help in three of the instances, in as much as the students did not show a preference for them. However, in the remaining three cases we found that it was the hospital that was at fault. They were late in forwarding their forms to the Canadian Intern Board in the first place, and in the second place their lists were not adequate. In one case all we received were the names of four men with no indication of which were preferred or which were alternate choices. In cases like this we usually informed the hospital of its mistake and asked it to give us the names of more men, if possible. However, in this particular instance the forms did not reach us until December 12th, about two weeks late and we were unable to act on such short notice.

The Canadian Intern Board is repeatedly endeavouring to impress upon the student the importance of acknowledging his appointment to the hospital after the final allotment. In a few instances they have failed to do so, but, at the time of writing, all have been acknowledged as far as we know.

Perhaps the most serious problem that the Canadian Intern Board faced this year was that of several of the hospitals announced their appointments and required those appointed to sign contracts before the announcement of the allocation by the Canadian Intern Board. In two or three instances, however, we were assured that it was due to a misunderstanding on the hospital's part and that it would not happen again next year. However, we are afraid that this was not so in every case. May we say, that there is absolutely nothing gained by this procedure, since if a student receives an appointment through the Canadian Intern Board later which he would rather have, as shown on his preference list, he usually decides to break his original contract. Once a student finds out that a certain hospital is breaking the rules, he will have few scruples about breaking his contract if he receives a better offer. This was one of the main drawbacks with the old system, and hospitals that do this are just defeating the purpose of the Board. However, we do believe that next year this will be all cleared up.

Likewise one deprecates the practice of certain hospitals forcing the students to divulge their order of preference. In nine cases out of ten the student will probably mislead the examiner, since he realizes that advantage is being taken of him. Those hospitals which practised this lost more than they gained, because they were so often misled by the student's answer.

In conclusion, the Canadian Intern Board has placed 188 interns in Canadian hospitals for the coming year directly and 11 more indirectly. It will endeavour to fill the quota of more hospitals next year, but from the above it can be seen that, unless some of the larger hospitals reduce their quota, the Canadian Intern Board will not be able to fill every hospital's requirements. However, we are sure that this shortage would have been just as great, and possibly greater, with the old system, and the confusion would have continued until Easter. As it is, all the appointments were made by December 15th, the students intend to fulfil their contracts and will not start to "bargain and shuffle" for another hospital in May or June, as so often happened in years gone by. Space has not permitted the presentation of an outline of the method by which the Board functions in this article, but if there is anyone who is not acquainted with these facts, kindly let us know and we will gladly forward the information.

The Secretary desires to express his gratitude to Dr. Harvey Agnew, Dr. Fred A. Logan, Dr. William Kerr for their generous assistance and sound advice. Without their help the Board could not have carried on.

CLIFFORD J. HEALY,
Secretary, Canadian Intern Board,
(University of Toronto, Meds. 4T1).

The War

Proceedings of the Canadian Medical Advisory Committee

The following items arising in recent meetings of the Canadian Medical Advisory Committee are published for the information of the members of the Association.

Foreign Exchange Control Board

By invitation, the Committee conferred with the Foreign Exchange Control Board, at which conference the Committee stated that the medical profession of Canada is qualified to provide adequate medical care for its people, thus making it unnecessary for Canadians to proceed outside of Canada for treatment. Your Committee was asked to provide a letter to be sent to every medical practitioner in Canada, setting forth the position which has been taken. This has been done.

The attention of the Committee was directed to a form of medical certificate issued by the Foreign Exchange Control Board, applicable to Canadian citizens who desire to go to the United States either for medical treatment or for reasons of health. In studying the form, the Committee felt that many of the questions requiring answers by the examining doctor might be deleted or separated to a second form, and so recommended. The form is being restudied by the Board.

Co-operation with the Air Force

The Committee interviewed the Honourable Mr. Power, Minister of Defence for Air, who accepted our offer of co-operation, and subsequently Group Captain Ryan, Senior Medical Officer in the Service, advised the respective P.M.O.'s in Canada to co-operate fully with the Advisory Committee of the Canadian Medical Association in respect to the selection of medical personnel for the Air Force.

Co-operation with the Navy

The Committee interviewed the Honourable Angus MacDonald, Minister of National Defence for Navy, offering the full co-operation of the Association in the selection of medical officers as required. Mr. MacDonald assured the Committee that in the further selection of medical officers for the Navy this Association will be consulted in matters which would properly come under our review.

It may be regarded as a matter of gratification that the Association has now formally and officially been recognized by the Three Departments of National Defence, to act in an advisory capacity coming within our scope and functions.

Enlisting of Interns

It is the Committee's understanding that the various services look favourably upon a recent medical graduate completing a year of junior internship before enlistment. Accordingly, enlistment of junior interns in the services will not be encouraged. There always remains, however, the matter of choice on the part of the individual, and the Committee is not in a position to guarantee that enlistment by junior interns will not take place.

Recruiting of Interns and Medical Students for Military Training

The Committee was assured by Major-General LaFlèche, Associate Deputy Minister of the Department of National War Services, that every consideration would be given interns and medical students in the selection of a time for their military training which would interfere as little as possible with their hospital and university obligations. As far as possible, the period of one year's internship will not be disturbed so long as the prospective trainee can take the training within twelve months of the date of proclamation calling out his age-group. Notification to this effect has been sent to hospitals and medical schools throughout Canada.

The following additional information was given to the Committee by Major-General LaFlèche:

1. *Categorization of prospective trainees* by original medical examiners was reasonably satisfactory but could be improved. The attention of the profession is redirected to the instructions sent to them. In this connection, Major-General LaFlèche provided the Committee with a letter to be published in our *Journal* and in Provincial Bulletins, the publication of which was approved by the Committee.

2. *Statistics re Rejections* due to physical unfitness are not yet ready for release, but it may be stated that the percentage is lower than might have been anticipated. When the break-down of statistics is available for publication full particulars will be supplied the Committee.

3. *Medical Advisers* have been selected and appointed by the Department of National War Services in the various Military Districts, part of whose duties will be to examine all medical certificates of trainees, with particular reference to rejections. An agreement was entered into between your Committee and Major-General LaFlèche by which the Canadian Medical Association, co-operating through its Divisions and the respective Colleges of Physicians and Surgeons, would undertake to nominate *Medical Boards* (three members to a Board—a physician, a surgeon, and an Eye, Ear, Nose and Throat specialist) for the purpose of re-examining recruits who were rejected at the first medical examination. On the nomination of the Canadian Medical Association the Boards will be appointed by the Minister, in the areas and to the number required, as set forth by the Minister. Each member of a Board will be paid $10 a day or $5 for part of a day, together with travelling

expenses where such are necessary when the Board is asked to proceed from its base. It is suggested that these Boards might be recruited from senior members of the profession who are less likely to be called upon for active military service due to age or some physical disability.

JOURNALS TO FIRST CANADIAN DIVISION MEDICAL SOCIETY IN ENGLAND

The members of the first Canadian Division Medical Society in England will be glad to receive current Medical Journals and Year Books. If any of our members can spare copies of these publications they will be performing a real piece of service by mailing them to the First Canadian Division Medical Society, Canadian Army Overseas.

MILITARY AND CIVIL MEDICAL NEEDS

It is recommended to all the Divisions that in the matter of enlistment of medical personnel for war services a careful watch be kept to provide a balance between military and civilian needs as related to medical practitioners.

JOURNALS TO MILITARY HOSPITALS IN CANADA

It has been decided that the *Canadian Medical Association Journal* will be sent, with the compliments of the Association, to the Military Hospitals in Canada of 250 beds and over, the list of such to be provided by the D.G.M.S.

It has been suggested that Medical Societies and members of the Association who are in possession of journals which they do not require for permanent preservation, might forward them to hospital units and medical personnel in military service, where they will be very much appreciated.

INDUSTRIAL MEDICINE

Some time ago the Committee had under consideration a proposal for the establishment of a Committee on Industrial Medicine, and the General Secretary was instructed to secure more detailed information on the proposal. The following suggestions were submitted:

1. That the attention of the Dominion Government, perhaps through the Minister of Munitions and Supply, be drawn to the contribution to the war effort which can be made by the medical profession through the practice of preventive medicine in war industry. This involved the employment by industry of physicians mainly on a retainer basis for work within the factory.

2. That an alternative might take the form of representation to Provincial Governments to pass regulations requiring employment by employers in war industry of physicians and nurses necessary for the maintenance of health. Such a measure is in effect in Great Britain. Expand the post-graduate training facilities of the Association to include industrial medicine, using short intensive courses in industrial centres to prepare physicians to meet the demand.

3. That a Committee on Industrial Medicine be appointed to consider and eventually to define the objectives and scope of industrial medicine; to consider the qualifications and training for industrial physicians and industrial nurses; and to make a survey of present personnel and training facilities.

It was the feeling of the committee that this matter was of sufficient importance to be studied by a Committee set up for the purpose; and it was agreed that Dr. J. G. Cunningham, of Toronto, and Dr. Vance Ward, of Montreal, be appointed a Committee with power to add, to study the question of Industrial Medicine and report back to the Executive Committee.

CENTRAL MEDICAL WAR COMMITTEE OF THE BRITISH MEDICAL ASSOCIATION

The Committee had before it a letter from the Central Medical War Committee of Great Britain requesting that 100 medical officers be recruited in Canada by the Canadian Medical Association for the R.A.M.C. The military authorities at Ottawa were conversant with the request.

In order that the Committee might consider this request thoroughly, it had available a list (in the various age-groups) of unmarried men who had already signified their willingness to proceed overseas; a list of those who had already joined one of the services; and an indication from the three military services as to the number of medical men who might be required during the course of the next twelve months. It was the unanimous opinion of the Committee that every endeavour should be made to secure for the R.A.M.C. at least 100 men as had been requested. The following procedure was agreed upon.

That the Divisions be acquainted with the request from the Central Medical War Committee of Great Britain by sending them a copy of the letter together with information *re* pay and allowances.

That there be sent to each Division information already available as to enlistments within the Division of unmarried men thirty years of age and under; that the Divisions be asked to check the enlistments against their records, noting the men not over thirty years of age, unmarried, who have volunteered to serve in any capacity overseas; and that inquiry be made of these men to ascertain if they would be willing to serve in the R.A.M.C.

If it is ascertained in such inquiry that a man has married since completing his registration card this information should be noted in the Divisional Records and communicated to the General Secretary.

It is hoped that it will not be necessary to disturb interns serving their first year in hos-

pital, nor that local medical services will be disrupted unduly.

That the Divisions be asked to take immediate action to ascertain the number of men not over 30 years of age and unmarried, who are licensed to practise, and who, in the opinion of the Division, are eligible to be recommended to the Canadian Medical Association for appointment in the R.A.M.C. according to the requirements herein specified.

All nominations from a Division are to be submitted to the General Secretary of the Canadian Medical Association who will arrange through the D.G.M.S. to have the candidates medically examined and documented to ascertain their fitness for service.

To secure at least 100 officers for the R.A.M.C. it seems wise to the Committee to ask for upwards of 125 nominations.

The General Secretary was authorized to carry out the arrangements discussed and agreed upon, as outlined herein.

The First Canadian Division Medical Society

The second meeting of the First Canadian Division Medical Society was held at a Main Dressing Station, somewhere in England, on November 12, 1940.

Many visitors were present from outside the Division. These included: Colonels G. Nasmith, L. Colebrook, R. M. Luton, J. A. Linton, C. L. Franklin, C. Fenwick, C. A. Rae, C. L. T. Arthur; and Lieut.-Colonels J. C. MacKenzie, J. T. Haszard, F. V. Williams.

A medical lending library was presented to the Society by Colonel George Nasmith. This was given in memory of the late Mrs. Nasmith through funds made available by the Heliconian Society in Toronto, of which she had been a valued member. Colonel McCusker accepted the gift on behalf of the members of the Society.

Colonel Leonard Colebrook gave an interesting paper on the use of sulfanilamide in the treatment of war wounds. Although experiments on animals had demonstrated that infections by *S. hæmolyticus* might be prevented if a sufficiently high concentration of sulfanilamide was maintained in the blood stream he did not feel that it was wise for the present to give a course of the drug to all wounded persons directly they become casualties. The high incidence of *S. hæmolyticus* infection which was associated with plastic surgery done on war wounds has decreased by 50 per cent following the administration of sulfanilamide before and after the operation. Similarly, the secondary *S. hæmolyticus* infections complicating severe burns responded rapidly to the exhibition of the drug. After a thorough debridement of infected war wounds and the liberal shaking of sulfanilamide powder on the surface they were covered by gauze moistened in normal saline. Following this procedure there was a rapid disappearance of *S. hæmolyticus* from the injured area.

Lieut.-Colonel H. M. Elder presented an interesting and instructive case. The soldier when living as a civilian in Montreal two years ago had been in a motor accident and had his right brachial artery and ulnar nerve severed. An anastomosis of the artery was done and heparin used to prevent clotting. The ulnar nerve was sutured. The results were so satisfactory that the young man was accepted as a recruit in the Canadian Active Service Force. At present the radial pulse is good and only a minimal ulnar paralysis remains.

A squad of stretcher bearers from one of the Canadian Field Ambulances then demonstrated the standard method of applying a Thomas splint, as outlined in the Royal Army Medical Corps Training Manual. This was followed by a demonstration of the application of a combination footpiece and support for use with the Thomas splint recently designed by Colonel E. A. McCusker. (A description of the use and advantages of this apparatus will be published later.)

Colonel R. M. Luton, Senior Medical Officer Overseas, Canadian Military Headquarters, and Colonel J. A. Linton, D.D.M.S., 7th Corps, spoke briefly. They both were interested in the subjects discussed during the afternoon, and indicated that additional arrangements were under consideration to keep the medical officers informed on various clinical problems.

The meeting then closed and a social half hour was spent.

A special clinical meeting was held at one of the English hospitals on November 27th. This particular hospital is being used as a Burn Centre for burn casualties from the three services. The afternoon was spent with the surgeon-in-charge, Mr. J. H. McIndoe, who gave a descriptive lecture on the etiology of war burns, their classification, first-aid measures, types of treatment, and the functional results.

The wards were then visited and an opportunity was afforded of seeing the results of various types of treatment. A demonstration was given of the warm normal saline bath which is being used at this centre for severe burns or for burns of special regions. The absence of pain during treatment, the shorter period for healing, and the good functional results were contrasted with the longer period for recovery and the variable functional results obtained after coagulation treatment with a tannic acid preparation.

It was therefore recommended that coagulation therapy be avoided for burns, involving the dermis or deeper structures of the face, hands, feet, flexures, and perineum.

A clinical day was held at No. 15 Canadian General Hospital on November 20th and at No. 5 Canadian General Hospital on November 27th. On each day, the staffs of the hospitals had

prepared a full program of interesting cases for presentation and discussion. Medical officers from the Division were present at both meetings.

The following officers have been on medical refresher courses for the month. Majors K. A. Hamilton, Royal Infirmary, Sheffield; F. B. Bowman and J. Boyd, Royal Infirmary, Edinburgh; Captain C. E. Holmes, Queen Victoria Cottage Hospital, East Grinstead; Captains J. K. Bell, H. T. Ewart, W. D. Samill, D. A. Young and A. S. Middlebro', Royal Infirmary, Edinburgh; and E. D. Rathbone, 5th Canadian General Hospital, Taplow.

Sphagnum

In the last war sphagnum moss was used fairly widely as an absorbent in wound dressings, and if casualties increase it may prove useful again. The large cells of the plant, which botanically lies between the true mosses and the liverworts, act as reservoirs and are perforated with small pores which allow the rapid absorption of water. Sphagnum is thus capable of taking up much more fluid than cotton-wool, in which the cellulose tubes are of small diameter, usually collapsed and twisted from drying, and incapable of filling by capillary attraction in the same way as the moss cells. A good sample of sphagnum will take up from 12 to 19 times its own weight of fluid and will hold up wound discharges until the whole mass becomes saturated. The conditions under which it is gathered and dried affect its absorptive powers considerably. It grows on damp moors and on lowland heaths and mosslands, and being easily recognized does not require experts to gather it. It is saturated with moisture when gathered and the natural impulse of the gatherers is to wring out the water before carrying the sack-load home, sometimes a distance of many miles; but this process is likely to damage the cellular structure and should be avoided if possible. The plants ought to be spread out in a sunny, airy place before the sack is filled, but since this is a counsel of perfection more often than not gentle squeezing may be necessary. When the gatherers reach home the collection should be spread out on the floor of a spare attic or outhouse to dry; but if a large demand for sphagnum arises it would be better to arrange depots in which the sphagnum could be dried on wooden or canvas trays arranged in racks separated sufficiently to allow of free circulation of air. The trays could be covered with butter-muslin and their contents dried in the open. Oven-drying is quicker, but makes the sphagnum brittle and less easy to handle. It should certainly not be dried in lofts over stables and shippens because of the danger of contamination with tetanus or other organisms. Once dried it can be stored in sacks for long periods without deteriorating. When required it should be picked over and any foreign bodies likely to promote the growth of fungi and any twigs or dead leaves should be removed; it should then be packed in muslin bags of fine mesh which will guard against dust. The full bags must of course be sterilized before being distributed as dressings. Steam at high or low pressure can be used for sterilization but it hardens the walls of the cells and reduces though it does not destroy their absorbing power; another method recommended is to charge the moss with gr. 17½ of corrosive sublimate to the pound, by soaking the bags in a solution of appropriate strength. Neither method seems ideal. During the last war large quantities of sphagnum were pressed into thin sheets in a hydraulic press and though these were convenient to handle the absorptive power of the sphagnum was impaired. Moreover, dressings made from such sheets were apt to swell, sometimes when there was no chance of adjusting the bandages. Sphagnum is a more serviceable dressing in the form of loose pads. Nurserymen have long used it as a packing for plants, but it would have to be collected more carefully for use as dressings. The gathering sites chosen should be unpolluted by smoke fumes from industrial works or by brackish water; the slopes below buildings and farms should be avoided because they may be contaminated by sewage. Possibly botanical and natural history societies could combine to supply manufacturers with moss sponsored by their members.—*The Lancet*, 1940, **2**: 753.

The Treatment of Frost-bite

Frost-bite, owing to the conditions of trench warfare in the winter months, was a frequent cause of disability during the war of 1914-18, but it has not reached serious proportions in the rather different circumstances of the present war. In the meantime some valuable contributions have been made to the study of peripheral vascular diseases and their treatment by sympathetic denervation. Three recent papers, all of them brief because the work was carried out under conditions of military necessity, make out a good case for fuller and more carefully controlled investigation of the treatment of frost-bite of the hands and feet on the lines of surgery of the sympathetic nervous system. Soupault and Orsoni[1] record a case of bilateral frost-bite of the feet which developed some days after prolonged exposure in the wet and cold. The feet were discoloured, œdematous, cold, and painful, and it was thought that a bilateral Syme's operation would be necessary. After a series of lumbar injections of syncaine there was a marked improvement in the local signs and the subjective symptoms, and ultimately the patient lost only the tips of three toes on one side and the tip of one on the other. Five similar cases recorded by Simon

1. *Mém. Acad. Chir.*, 1940, **66**: 358.

and Filhoulaud,[2] none of them as severe as many seen during the last war, did not come under observation for seven to nine days after the onset of the frost-bite. Two were treated by lumbar injections of novocain and the others by femoral sympathectomy. Good circulatory responses were obtained in all, and it is claimed that necrosis was thereby limited and healing facilitated. Forster and Wiederkehr[3] report the case of a patient who developed frost-bite in one hand after motor-cycling in intense cold and came under observation eight days later. The stellar ganglion was injected by the method of Leriche and Fontaine; vasodilatation, diminution in the swelling and pain, and rapid healing followed. Under conditions of warfare frost-bite is likely to attack young men with healthy arteries—that is, excellent subjects for surgery of the sympathetic nervous system. An approach on these lines is a rational one, since the smaller arterioles are in a state of spasm. At the same time the gangrenous process is one which spreads from the surface towards the deeper tissues. The elimination of vasoconstriction may in the early stages prevent the onset of gangrene, or, when gangrene is established, may limit its spread, diminish pain, assist in the separation of dead tissue, and promote healing.—*Brit. M. J.*, 1941, **1**: 21.

Medical Aid from the United States

The *Journal of the American Medical Association* announces that forty-eight physicians have formed a medical and surgical supply committee, with offices at 420, Lexington Avenue, New York, and undertaken a nation-wide campaign for surgical and medical supplies to equip 500 first-aid stations and field hospitals to help in caring for the British war wounded.

Civilian Deaths from Military Action

Before the present European war the prediction was freely made by military and political experts that entire cities would be laid waste speedily and completely by aerial bombardment, with enormous losses of civilian lives. Fortunately, this dire prediction has not been borne out by the course of events. Heavy as losses of life have been from this cause, the numbers reported do not compare with the forecasts. Nevertheless, in the present war, civilian losses of life arising from military operations have been distinctly greater than in the World War, particularly in comparison with the number of deaths in the armed forces. These civilian losses have been high not only from air raids, but also from direct gunfire, which was experienced at its worst in Polish cities, particularly Warsaw, and on the refugee-choked roads of Belgium and northern France. Another source of severe loss of life among civilians has been in the sinking of ships.

2. *Ibid.*, 359.
3. *Ibid.*, 367.

It is impossible to secure up-to-date or reliable information on the numbers of lives lost, either military or civilian, but even the fragmentary data available reveal the changed picture with respect to the number and causes of civilian casualties.

As a background, it will be well to recall the pertinent facts of the World War. Then, the military losses were huge as compared with today's figures. From 1914 to 1918, deaths from military action in the armed forces of the belligerent countries were at least 7,000,000. On all fronts in the present war, or series of wars, including that between Russia and Finland, deaths in action in the army, navy, and air forces combined may well be in the neighbourhood of 300,000. This figure is not much greater than the military losses of Germany in 1914 alone. It is certainly smaller than the losses of life for both sides on the western front during the first few months of the World War.

Deaths of civilians during the World War, due directly to air raid, gun or artillery fire, or sinking of ships, were small, as compared with the figures for the armed forces. These civilian losses, including those of neutral nations, have been estimated to be in the neighbourhood of 100,000 for the period 1914-1918. How this estimate was made and how accurate it may be is uncertain, but it appears reasonable, judging by available figures for certain types of losses.

In the World War the deaths of civilians in airplane and airship raids numbered 1,117 for Britain, 746 for Germany, and 965 for Italy. French losses were higher. They were greatest in cities in the combat areas, where no competent records were available. In Dunkirk alone, however, 427 deaths occurred as a result of air raids; and in Paris, 266. Data on civilian losses of life by artillery or gunfire or shellfire from ships are even more fragmentary. About 1,000 English civilians were killed, or died as a result of naval shelling or other enemy action, exclusive of air raids. In French cities, Reims counted the most victims, in excess of 1,000, and Lens was next, with more than 500 dead. Paris suffered 256 fatalities as a result of long-range artillery fire, 88 of them from a single shell that hit a church.

The other major source of direct casualties among civilians was the sinking of ships. English losses of sailors in merchant or fishing vessels amounted to 15,313; the French losses were 1,440; and the Italian, 1,361. The number of civilian passengers lost is not known, but reached a considerable figure. Passenger losses on the *Lusitania* alone were 785 in number.

The number of civilian deaths in the present war are in painful contrast with these earlier figures. It is likely that they already exceed the figures of the World War, although reasonably accurate figures are available only for certain areas. Of the chief countries at war, Britain's data are probably the most reliable,

with reported deaths in air raids totalling nearly 20,000 up to the end of November 1940. Figures on her losses of sailors on commercial vessels are not available, but they certainly run into four figures. Passenger losses have also been numerous, though much less than among sailors.

The heaviest losses of life among civilians have occurred on the continent—in Poland, where Warsaw's dead alone were estimated at 50,000; in Belgium and northern France, where refugee casualties have been estimated to exceed 40,000, with an unknown but certainly a considerable number of deaths; and the huge civilian mortality in Rotterdam, which was reported to reach 30,000. Civilian deaths from air raids in Germany and Italy are not known with any exactness, but they are small as compared with these other figures. Likewise, only fragmentary data exist about losses of life of civilians in Belgian and French cities and towns during air raids and bombardments.

From the data at hand, it is likely that already more than 100,000 civilians have died in the present war as a result of bombardment by land, sea, and air. While these civilian deaths do not exceed those among the military forces, being probably in the approximate ratio of 1 to 3, the situation is distinctly different from the World War when the ratio was of the order of 1 to 75. What lies ahead no one really knows, but it is likely that the ratio of direct civilian casualties will remain comparatively high. Large as these losses of life are, it is clear that they are far lower than many experts had predicted. Indeed, the casualties from spectacular air raids should not blind officials to the far more serious threat from silent enemies—epidemic diseases resulting from or associated with crowding in air-raid shelters in large cities, the breakdown of sanitary facilities, the pollution of water supplies, and the weakening of resistance by hunger and cold. While sporadic outbreaks of such diseases have occurred, and there have been unauthenticated reports of some serious ones, the danger of much more disastrous epidemics is very real, and neutral countries will probably not escape their ravages. We can only watch and wait.—Reprinted from the *Statistical Bulletin*, Metropolitan Life Insurance Company.

War Literature

THE BRITISH MEDICAL JOURNAL

Immunization against Infection in the Army, Lt.-Col. H. J. Bensted, 1941, **1**: 18.

Cerebrospinal Meningitis: The Use of Sulphonamide Derivatives in Prophylaxis, R. W. Fairbrother, 1940, **2**: 859.

Hospital Infection of War Wounds, A. A. Miles and others, 1940, **2**: 855, 891.

Blood Changes in Vitro (Annotation), 1941, **1**: 58.

JOURNAL OF THE ROYAL ARMY MEDICAL CORPS

The War and Ourselves, F. A. E. Crew, 1940, **75**: 345.

SURGERY, GYNÆCOLOGY AND OBSTETRICS

The Surgery of Modern Warfare, F. A. Coller and J. M. Farris, 1941, **72**: 15.

THE LANCET

War Strain (Discussion), 1940, **2**: 756.

A Wartime Pharmacopœia, M. H. Papworth, 1941, **1**: 3.

THE PRACTITIONER

Common Winter Disorders of the Nose and Throat among the Services under War Conditions, H. V. Shea, 1940, **145**: 316. (Abstracted in the February issue of the *Canad. M. Ass. J.*, p. 200.)

BOOKS AND PAMPHLETS

Health of Munition Workers, H. M. Vernon, Oxford University Press, London, 1940. Price 8/6 net.

War Wounds and Injuries, Edited by E. Fletcher and R. W. Raven, Edward Arnold & Co., London, 1940. Price 14s. net.

Medical Diseases of the War, Sir Arthur Hurst, London, Edward Arnold & Co., 1940, 16s.

The Surgery of Injury and Plastic Repair, Samuel Fomon, London, Baillière, Tindall & Cox, 1940, 94s. net.

Emergency Surgery, Hamilton Bailey, Bristol, John Wright & Sons Ltd., 1940, 63s. net.

Bulletin of War Medicine, (contains abstracts of recent articles in all branches of medicine, surgery, and kindred subjects; very complete). H. M. Stationery Office, London, 1940. Price 2/6.

Divisions of the Association

Canadian Medical Association, Saskatchewan Division

The following chairmen of committees and members of corresponding committees of the Canadian Medical Association were chosen at the annual meeting of the Council of the College of Physicians and Surgeons held November 30, 1940.

Archives—Dr. J. A. Valens, Saskatoon; *Cancer*—Dr. E. B. Alport, Regina; *Constitution and By-laws*—Dr. O. E. Rothwell, Regina; *Legislation*—Dr. W. A. Dakin, Regina; *Economics*—Dr. D. P. Miller, Prince Albert; *Maternal Welfare*—Dr. Lillian A. Chase, Regina; *Medical Education*—Dr. W. S. Lindsay, Saskatoon; *Pharmacy*—Dr. M. Powers, Regina; *Public Health*—Dr. A. Wilson, Saskatoon; *Credentials and Ethics*—Dr. J. F. Irving, Yorkton; *Nutrition*—Dr. J. Orr, Moose Jaw; *Post-graduate*—Dr. C. R. May, Regina.

LILLIAN A. CHASE

Medical Societies

Société médicale des hôpitaux universitaires de Québec

La Société Médicale des Hôpitaux Universitaires de Québec tenait, le 17 janvier 1941, à la Faculté de Médecine, son assemblée générale annuelle au cours de laquelle on procéda à l'élection du bureau exécutif pour l'année 1941. Le nouvel exécutif se compose comme suit: *Président*—M. Joseph Caouette, M.D.; *Vice-président*—M. Roland Desmeules, M.D.; *Secrétaire*—M. Richard Lessard, M.D.; *Trésorier*—M. Marcel Langlois, M.D. *Directeurs*—M.

Charles Vézina, M.D.; M. A. R. Potvin, M.D.; M. Sylvio Caron, M.D.

Le secrétaire, le docteur R. Desmeules, donna lecture du rapport annuel de la Société. Au cours de l'année 1940, il y eut 13 séances et 48 travaux furent présentés.

Le trésorier, le docteur Gustave Desrochers, dépose son rapport annuel qui est accepté.

Le docteur Gingras présente le rapport de la revue "Laval Médical".

A la fin de la réunion, le président sortant de charge, le docteur Edmour Perron, remercie ses confrères de la confiance qu'ils lui ont manifestée en l'élisant président d'une société qui eut pour la diriger les docteurs Arthur Rousseau, J. Guérard, P. Calixte Dagneau et Arthur Vallée.

R. DESMEULES, M.D.,
Vice-président.

La Société de Gastro-entérologie de Montréal

La Société de Gastro-entérologie de Montréal a élu pour 1941 le Conseil suivant: *Président:* Dr Pierre Smith; *1ier vice-président:* Dr Mercier Fauteux; *2ième vice-président:* Dr Jean LeSage; *secrétaire:* Dr Roger Dufresne; *trésorier:* Dr A. Cantero.

La Société Médicale à l'hôpital Notre-Dame, de Montréal

A sa séance du 3 décembre dernier la Société Médicale de Montréal étudiait et discutait la grande question médico-sociale du rachitisme. Le Dr J. A. Baudouin présenta la prophylaxie de cette maladie; le Dr Willie Major, son traitement médical, et le Dr J. E. Samson son traitement chirurgical. Les lecteurs intéressés trouveront un compte-rendu de cette séance dans *l'Union Médicale,* Vol. 70: 2 (fév. 207-208), 1941.

La Société exprimait le vœu que soit intensifiée la lutte contre le rachitisme et demandait à la population de coopérer davantage dans ce sens avec les pouvoirs publics, les institutions hospitalières, et la profession médicale; elle conseillait, comme moyen de prophylaxie, un contrôle périodique de l'alimentation des nourrissons, à l'aide d'examens médicaux bien suivis, et l'administration régulière de vitamine D aux jeunes enfants pendant l'hiver.

University Notes

University of Western Ontario

Dr. William W. Bryan has been appointed Professor of Radiology in the University of Western Ontario Medical School and Radiologist at the Victoria Hospital, London, Ont.

Following his graduation from the Emory University, Atlanta, Georgia, Dr. Bryan served as House Officer in the Jackson Memorial Hospital, Miami, Florida, during 1932 and 1933. He was House Officer and Resident in Radiology at the Peter Bent Brigham Hospital, Boston, under Dr. Merrill C. Sosman, from 1933 until 1935, and was assistant in Radiology at the Harvard University Medical School in 1934 and 1935. He was Roentgenologist at the Grady Hospital, Atlanta, Georgia and Instructor in Surgery (Radiology) in the Emory University School of Medicine 1935 to 1937. Since that time Dr. Bryan has been Assistant Radiologist at the Royal Victoria Hospital, Montreal (1937 to 1940) and Assistant Demonstrator of Radiology in McGill University from 1938 to 1940.

Abstracts from Current Literature

Medicine

Considérations sur 179 cas d'ulcère gastro-duodenal traités a l'Hotel-Dieu de Québec au cours des années 1937-38-39. Jobin, J. B. and Duval, J. P.: *L'Union Médicale du Canada,* 1941, **70**: 8.

In this interesting work the authors state the conclusions at which they have arrived, as follows:

The good result from treatment with histidin as an adjuvant to other measures.

Physical and mental rest in addition to dietetic and medicinal measures.

The harmful rôle of overwork and the abuse of tobacco in promoting new attacks and complications.

The medical treatment of hæmatemesis is to be preferred to the surgical, since the latter carries with it a higher mortality.

Early surgical intervention in cases of perforation and the importance of recognizing slow perforation without the classical sign of "wooden stomach".

The considerable value of pre-operative treatment in cases of stenosis, gastric intubation, lavage with collargol, with injection of a solution of atropin 1:4,000.

The search for a neoplastic transformation of a gastric ulcer under the close collaboration of physician, radiologist, and gastroscopist.

Surgical measures are indicated in cases of ulcer which have resisted a thoroughly carried out medical treatment. YVES CHAPUT

Carbohydrate Metabolism in Addison's Disease. Thom, G. W., *et al.*: *J. Clin. Invest.,* 1940, **19**: 813.

A high proportion of untreated patients with Addison's disease were observed to have a disturbed carbohydrate metabolism. This defect can be most readily demonstrated by the application of a standard intravenous glucose tolerance test. The abnormality in carbohydrate

metabolism appeared to be specific, since it persisted despite the correction of the disturbance in electrolyte balance, plasma volume, and blood pressure by means of desoxycorticosterone acetate therapy. Treatment with quantities of adrenal cortical extract, 17-hydroxy-11-dehydrocorticosterone (compound E) and corticosterone, in order of potency, corrected the abnormal carbohydrate metabolism.

S. R. TOWNSEND

The Incidence of Aspirin Hypersensitivity. Gardner, E. and Blanton, W. B.: *Am. J. M. Sc.*, 1940, **200**: 390.

The authors have reviewed the histories of 467 patients consulting the Department of Immunology, Medical College of Virginia, in order to determine the incidence of aspirin hypersensitivity. More than half of the patients were asthmatics and all had some sort of allergy. Five patients in this group were found to be mildly hypersensitive to aspirin. Two of these developed asthmatic attacks after taking the drug; and two, angioneurotic œdema. None developed dangerous or alarming symptoms.

A questionnaire sent to some 22 physicians throughout the United States showed that 170 out of 90,000 patients exhibited some form of hypersensitivity. In this group there were 71 instances of quinine sensitivity. Considering the fact that there is only about 1/17th as much quinine as aspirin consumed, it may be deduced that the chances of an individual being sensitive to quinine are seven times as great as for aspirin.

The authors conclude that not more than two out of 1,000 persons are sensitive to aspirin, and the probability is that these will not react violently to it.

E. S. MILLS

Surgery

A Statistical Study of Post-operative Venous Thrombosis and pulmonary Embolism. 1. Incidence in Various Types of Operation. Barker, N. W., *et al.*: *Proc. Soc. Staff Meet., Mayo Clinic,* 1940, **15**: 769.

A statistical study of the incidence of post-operative venous thrombosis and pulmonary embolism in various types of operations indicates that the complications are more common following types of laporotomy in which operations on the female pelvic organs are done, in which there may be injury to or ligation of branches of the iliac veins; that they are more common in operations of long duration and of great magnitude, in which considerable tissue is removed and in which there is likely to be a greater amount of tissue injury; and that they are more common in patients with carcinoma and in conditions in which there is infection.

The authors do not wish to minimize the seriousness of post-operative venous thrombosis and pulmonary embolism, but point out that, taking all operations together, the incidence in their large series was only about 1 per cent. Even following splenectomy, in which the complication of venous thrombosis or pulmonary embolism is most frequent, the incidence was only 5 per cent, and the highest incidence of fatal pulmonary embolism following any type of operation was only 0.77 per cent. The actual differences between the incidence in various types of operations are comparatively small. Any program for preventive treatment of post-operative thrombosis and embolism must take into consideration the fact that the incidence of these complications is small even in operations such as splenectomy, hysterectomy, and resections of the stomach or bowel, and of necessity such a program must be used in several thousand consecutive cases before its effectiveness can be truly evaluated.

S. R. TOWNSEND

Partial Gastrectomy for Duodenal Ulcer: A report of 212 cases. Lewis, E. B. and Lemon, R. G.: *Proc. Staff Meet. of the Mayo Clinic,* 1940, **15**: 765.

Les auteurs rapportent deux cent douze malades porteurs d'ulcère duodénal, ayant subi une gastrectomie partielle, type Polya, chez qui un tiers ou plus de l'estomac fut reséqué. Aucun n'ayant subi une gastro-entérostomie ou une gastrectomie partielle antérieurement. Mortalité post-opératoire de 1.9 pour cent soit quatre décès.

Ayant pu retracer 197 de ces malades, les auteurs présentent les résultats suivants: 83.5 pour cent ne présentent aucun trouble digestif; 14 pour cent doivent diminuer leurs activités et faire quelques restrictions alimentaires; 2.5 pour cent souffrent d'ulcère jéjunal anastomatique ou peptique (nomenclature française).

Après gastrectomie, de 63 à 80 pour cent présentent une anacidité gastrique.

YVES CHAPUT

Current Methods in the Management of Peptic Ulcer. Hunt, V. C.: *Surg., Gyn. & Obst.,* 1940, **70**: 319.

Trois périodes caractérisent l'évolution du traitement chirurgical de l'ulcère gastro-duodénal. De 1885 à 1910 environ, période d'initiation chirurgicale; de 1910 à 1930 environ, période d'une chirurgie mieux conçue à la lumière des acquisitions physiologiques; de 1930 à nos jours, cette chirurgie est étayée sur une plus entière compréhension des modalités, des résultats et des procédés chirurgicaux couramment employés.

S'il semble admis que l'ulcère n'est pas une maladie exclusive, mais plutôt une manifestation gastro-duodénale d'un état fonctionnel anormal, il est non moins vrai que le traitement habituel se dirige vers la manifestation locale, c'est à dire, l'ulcère, et que le traitement médical ou chirurgical cherche à contrôler la

sécrétion gastrique acide soit en la diluant ou en la neutralisant, soit en le diminuant.

Indications chirurgicales dans l'ulcère gastro-duodénal.—Les résultats du traitement médical éclairé sont excellents dans maints cas d'ulcères gastro-duodénaux non compliqués, lorsque surtout les manifestations symptômatiques sont brêves; moins bons, si l'ulcère est passé à la chronicité.

Ici, l'auteur rend compte des données actuelles sur les résultats du traitement médical, appuyées sur des statistiques récentes.

L'opinion commune actuelle concernant le traitement chirurgical est la suivante: relèvent de la chirurgie, tout ulcère ayant résisté au traitement médical suivi; les ulcères perforés en péritoine libre ou recouverts, les ulcères avec rétention gastrique, les ulcères hémorragiques graves, l'ulcéro-cancer. L'auteur pose les indications chirurgicales et fait des commentaires sur le diagnostic, la thérapeutique, et les indications chirurgicales dans ces cas.

Les Procédés chirurgicaux: peuvent se ramener à trois principaux: (1) indirect; gastro-entérostomie et gastro-duodénostomie avec ou sans exclusion du pylore. (2) opérations plastiques sur le pylore avec ou sans excision de l'ulcère. (3) résections gastriques diverses avec leurs différents modes de restauration de la continuité du conduit gastro-intestinal.

L'auteur rappelle les indications de chacun de ces procédés principaux avec leurs variantes opératoires utilisables suivant les lésions, en indiquant les résultats basés sur les compte-rendus et les statistiques d'auteurs connus et sur ses constatations personnelles.

A remarquer notamment que maints chirurgiens tendent actuellement à pratiquer la gastrectomie dans les cas d'ulcères duodénaux simples ou hémorragiques, ce procédé quoique plus grave diminuant les chances d'apparition de l'ulcère anastomotique, c'est à dire de l'ulcère peptique.

Aucun procédé cependant ne doit être utilisé de façon routinière, mais il faut s'appliquer à trouver le plus efficace et le moins dangereux pour chaque cas particulier. PIERRE SMITH

Obstetrics and Gynæcology

Lactation and Breast Feeding. Hunter, W.: *Brit. M. J.*, 1941, **1**: 827.

Breast feeding offers the child the best chances of survival and good health, and contraindications to natural feeding are few. Breast development is brought about by the action of œstrin and progestin, and secretion of milk follows withdrawal of the ovarian hormones, the secretion of prolactin and breast stimulation by the sucking reflex.

The general care of the patient and proper management of the breasts are of considerable importance during the ante-natal period as well as during the suckling. Regular feeding and the complete emptying of the breasts are essential, and test feeding is the most reliable index of breast function.

Deficiency of breast secretion should be treated by instituting a suitable feeding routine, improving the general health of the mother, and preventing excitement and worry so far as is possible. Smoking is prohibited, dehydrating aperients are avoided, and an adequate fluid intake is given. Both breasts may be used for each feed, and vitamin E and prolactin may be administered with advantage.

The mental attitude of the mother towards breast-feeding is most important, and she should be given every encouragement in her efforts to feed the child.

When suppression of lactation is desired, the mother's fluid intake is reduced, the breasts are bound, and œstrin is given. Breast discomfort may be relieved by mild sedatives or partial emptying of the glands when necessary.

ROSS MITCHELL

The Diagnostic Value of Pregnandiol Excretion in Pregnancy Disorders. Cope, C. L.: *Brit. M. J.*, 1940, **2**: 545.

Pregnandiol is a product of corpus luteum and placental metabolism. Its excretion in the urine is relatively easily measured in any biochemical laboratory. An attempt has been made to assess the diagnostic value of pregnandiol excretion in abnormal pregnancy. Its complete absence is nearly always evidence of serious abnormality, suggesting in early pregnancy the death of the fetus. The significance of a low pregnandiol excretion still remains uncertain. A normal pregnandiol excretion is not evidence that abortion will not occur or that the fetus is still alive. Both chronic nephritis and toxæmia of pregnancy may interfere with pregnandiol excretion. Deviation from the normal excretion in these conditions does not necessarily mean that gestation is abnormal. Pregnandiol excretion seems assured of a place as a diagnostic aid in obstetric disorders. ROSS MITCHELL

Clinical Ulcerative Vulvitis and Stomatitis. Jones, O. V.: *J. Obst. & Gyn. of the Brit. Emp.*, 1940, **47**: 557.

Cases of ulcerative vulvitis are not unusual. In the majority of the cases, however, there has been no question concerning the etiology of the condition, either infectious conditions such as diphtheria, gonorrhœa and pneumonia, or blood dyscrasias such as purpura and agranulocytic angina, being certainly responsible.

Since the original description in 1895, several cases have been reported in which there were co-existing ulcers in the mouth and on the external genitalia, but so far as review of the literature permits only 3 can be identified as having in addition some relation to menstruation.

In the case reported the vulvar lesion commenced 1 to 2 weeks before menstruation, last-

ing over the period but ceasing after menstruation, while the mouth lesion occurred 1 to 2 days before, during or after menstruation.

It may be noted that the lesions are present during the stage when the pituitary normally lessens its production of prolans and that their absence is coincident with the interval when anterior pituitary reaches its maximum concentration. Likewise during pregnancy (Ziserman's case) when the anterior pituitary hormone attains its highest degree of activity, there was a spontaneous disappearance of the ulceration. It, therefore, seems reasonable to suggest that a lowered pituitary activity is the cause of this condition. P. J. KEARNS

Ophthalmology

A Simple Method of Localizing Large Retinal Tears. McAlester, A. W.: *Am. J. Ophthal.*, 1940, **23**: 1161.

The apparatus necessary is a soft rubber dropper bulb, and an ordinary finger flash light. The eye is cocainized, and the pupil is widely dilated. The large end of the rubber bulb is placed over the cornea. When large tears or disinsertions are present, there will be a difference in the shadow that is reflected through the sclera. The procedure is more satisfactory for tears in the upper part of the globe than in the lower. We have not found it to be of any value in small tears. The examination obviously is carried on in a dark room. S. HANFORD MCKEE

A Study of Practical Cycloplegia, with Special Reference to the Use of Paredrine: A review of 341 cases. Wenaas, E. J., Evans, W. H. and Odom, R. E.: *Am. J. Ophthal.*, 1940, **23**: 1123.

In the last few years, the use of benzedrine or paredrine as an adjunct in the production of cycloplegia by atropine or homatropine has been recommended by a number of investigators, who claim that these adrenergic compounds exert a synergistic action that heightens the cycloplegic effect of atropine and its derivative. In several studies the conclusion has been reached that when these drugs are used as adjuvants smaller quantities of the cycloplegic are required to depress accommodation, and that the period of accommodated disability after refraction is shortened.

Detailed studies in a series of 341 cases show that paredrine has no advantage as an adjunct in the production of satisfactory cycloplegia. Neither does it influence the period of accommodated disability following cycloplegia. It has some value in producing mydriasis in conjunction with euphthalmine in aged patients. These studies show that satisfactory cycloplegia can be produced with minimum quantities of homatropine and atropine, and that smaller quantities have an advantage in shortening the period of accommodative disability. The quantity of the cycloplegic used should be individualized and not administered by a blanket formula. S. HANFORD MCKEE

Neurology and Psychiatry

Migraine Equivalents. Slight, D. and Morrison, D. A. R.: *Am. J. of Psychiat.*, 1940, **97**: 623.

The meaning of equivalents is defined and their importance is indicated. This series comprises 169 cases of migraine in which equivalents occurred in 52 (30.8 per cent). In 25 cases the equivalents replaced the classical syndrome of headache, nausea and vomiting, and visual disturbances.

It is concluded that equivalents may replace migraine entirely and be episodic or continued in form, or may alternate with migraine attacks in episodic form. The equivalents lend support to the theory that migraine is the result of an imbalance between processes of excitation and capacities for external "discharge". Whereas the former is dependent upon constitutional factors, the latter is determined largely by factors of training and experience affecting the organization of the nervous system. Equivalents occur in migraine in relation to alterations in intensity of the nervous processes involved, as dependent on external factors of stress or to changes in the affector—effector balance. The specific form of some equivalents is presumably dependent upon constitutional factors.

GILBERT ADAMSON

A Thirteen Year Follow-up Study of a Series of Cases of Verified Tumours of the Brain. Davidoff, L. M.: *Arch. Neurol. & Psychiat.*, 1940, **44**: 1246.

The late results in 152 verified cases of tumour of the brain on which Dr. Cushing performed operation in 1925-1926 are reported. Twenty-three of the patients died before leaving the hospital. Eighty-one died in from a few months to seventeen years after the first operation. Forty-five were still alive and most of them well, at the time of this survey, from thirteen to more than fourteen years after operation. The author discusses the average survival period and the period of useful activity after operation in the various tumour types. Glioma included the least favourable as well as the most favourable lesions in the whole series. The general impression was gained that improvement in the future treatment of tumours of the brain must take two directions; in the case of benign tumours, technical improvement to make surgical removal more complete and less hazardous; and in the case of malignant tumours, some form of therapy other than surgical. FRANK TURNBULL

Dermatology

An Interpretation of Bruusgaard's Paper on the Fate of Untreated Syphilitics. Sowder, W. T.: *Am. J. of Syph., Gon. & Ven. Dis.*, 1940, **24**: 684.

For a twenty-year period, 1891 to 1910 inclusive, at the Riks Hospital in Oslo little or no specific antisyphilitic treatment was given to patients with early syphilis, since Prof. C. Boeck, the clinic chief at that time, was of the opinion that the human body was better able to overcome the harmful effects of syphilis if the host-parasite was uninterfered with by the drugs then available: potassium iodide and mercury. In 1925 Bruusgaard, Boeck's successor, made an effort to determine the fate of these persons.

Of the 2,181 cases of primary and secondary syphilis admitted to the clinic in the twenty-year period, 473 (22 per cent) were traced and investigated. They had had syphilis for three to forty years. Presumably none of them had had any antisyphilitic treatment.

Of the 473 patients 309 were still living in 1925 when Bruusgaard published his report. Two hundred were well clinically, although 68 still had positive serological tests of the blood; 58 had benign tertiary lesions of the skin, mucosæ or bones; 21 had cardiovascular disease, presumed to be syphilitic; 25 showed clinical signs of paresis, tabes or cerebrospinal syphilis; 1 had aortic aneurysm and tabes; 6 were insane (whether or not from syphilis is not stated).

Sowder has subjected this report to a critical analysis and his conclusions are that more selection took place in the cases followed by Bruusgaard than is commonly supposed, and that the direction of this selection has been to exaggerate the seriousness of the disease rather than to minimize it. The reasons for these conclusions make up the bulk of Sowder's paper and justify its study by those interested.

D. E. H. CLEVELAND

Therapeutics

Clinical Experience with Sulfamethylthiazole. Brown, A. E. and Herrell, W. E.: *Am. J. M. Sc.*, 1940, **200**: 618.

The authors review their clinical experience with the use of sulfamethylthiazole in 30 cases of pneumonia, 7 of septicæmia, 5 of acute bacterial endocarditis, 5 pelvic infections, 4 osseous infections, 25 cutaneous infections, 13 infections of the ear, nose, and throat, 3 urinary infections, and 14 cases of miscellaneous infections; a total of 106 cases. The drug was administered orally to the majority of the patients in doses similar to those of sulfanilamide and sulfapyridine. However larger doses were frequently used for and tolerated by the severely ill patients. The sodium salt of sulfamethylthiazole was used intravenously for three patients, and it significantly elevated the concentration of the drug in the blood. Sulfamethylthiazole orally produced concentrations of the free drug in the blood similar to but somewhat lower than those that result from sulfapyridine. A minimal amount of conjugation occurred with sulfamethylthiazole. The results obtained to date from its use seem to substantiate experimental predictions. *Staph. aureus* and *Diplo. pneumoniæ*, type I, infections in particular seem to respond to treatment. With the exception of lower motor neurone involvement in 3 cases, and of cutaneous eruptions in 9, toxic effects seem to be less than those encountered following the use of sulfapyridine and sulfanilamide. Significant nausea and emesis occurred infrequently. The danger of lower motor neurone involvement makes it unwise to use sulfamethylthiazole for mild infections caused by *Staph. aureus*. However, a fulminating infection which carries a high mortality rate far outweighs the danger of toxic manifestations from drug therapy, and this drug or a related preparation may be indicated.

S. R. TOWNSEND

The Effect of Sulphanilamide Compounds on Endocarditis. Major, R. H.: *Am. J. M. Sc.*, 1940, **199**: 759.

In this paper Major compares the results of treating seven cases of endocarditis lenta by means of sulfanilamide or one of its compounds with a previous series of 15 cases, all fatal. In his second series of seven cases only four died, either directly or indirectly, from the disease. Three cases apparently recovered.

Promptly after beginning treatment the fever disappeared, the spleen shrank in size, and the blood stream became sterile. In one instance the drugs used were sulfanilamide and prontosil; in the second, prontosil and neoprontosil; and in the third, sulfapyridine. Two of the cases showed a persistently normal sedimentation rate after treatment and were in good health almost a year later. The third cured case died of cardiac failure two months after discharge from hospital. Sections of the valves showed a healing process and no organisms could be cultured from them.

The author admits freely that his series of cures is small and that insufficient time has elapsed since treatment was instituted.

E. S. MILLS

The Combined Use of Ouabain and Digitalis in the Treatment of Congestive Heart Failure. Batterman, R. C., Rose, O. A. and DeGraff, A. C.: *Am. Heart J.*, 1940, **20**: 443.

The authors present a carefully selected and controlled series of sixty digitalizations with an initial dose of 0.5 mg. (5 cat units) of ouabain intravenously and a simultaneous dose of 6 to 8 cat units of digitalis leaf orally. No further glucoside is given for 24 hours, at which time

the patient is placed on a daily maintainance dose of one to two cat units of digitalis leaf by mouth. They point out that the rationale of this method is based on the premise that the rapid therapeutic effect and quick elimination of ouabain, when combined with the slower but more prolonged effect of digitalis, would result in a rapid but prolonged glucoside effect.

In the majority of these cases, improvement occurred within one hour, and this improvement, once established, was progressive. The maximum effect was attained at the end of twenty-four hours. Rheumatic and hypertensive cases showed the highest incidence of early (within one hour) improvement. They found that after the initial digitalization, it was not difficult to establish the maintenance dose of digitalis leaf. One-fifth of the cases had auricular fibrillation, the remainder sinus rhythm, and the method was found to be applicable in both types of cases.

Evidences of toxicity were the least that could be expected; 18 per cent showed some manifestation of this, as evidenced by anorexia, nausea, vomiting, or a prolonged P R interval of the electrocardiogram. They were able to correlate toxic symptoms with the dosage of digitalis leaf given, and from this suggest the initial dosage of 4 cat units of digitalis leaf for patients weighing less than 125 lbs., 6 cat units for those weighing 125 to 175 lbs., and 8 cat units for those over 175 lbs. W. H. HATFIELD

Pathology and Experimental Medicine

Pathologic Changes Following Prolonged Administration of Sulfathiazole and Sulfapyridine. Rake, G., van Dyke, H. B. and Corwin, W. C.: *Am. J. M. Sc.*, 1940, **200**: 353.

The authors have investigated the toxicity of sulfathiazole and sulfapyridine by administering the drugs to mice, rats, and monkeys. Sulfathiazole, when given as 2 per cent of the diet (an amount necessary to produce bacteriostatic effects), killed 77 per cent of mice during a four-week period and produced lesions in the spleen, liver, and genito-urinary tract. These changes consisted of cloudy swelling of the liver and disorganization of the germinal centres in the spleen. In the kidney two types of lesions were encountered. In addition to the mechanical blocking of ureters and pelvis by concretions of crystals of the drug (25 per cent free and 75 per cent conjugated), there occurred damage to the glomeruli and hyaline necrosis of the lining cells of the convoluted tubules. Sulfapyridine was not lethal and produced fewer pathological changes. On the other hand, sulfapyridine appeared to be twice as harmful to rats as sulfathiazole.

In monkeys receiving a single daily dose by stomach tube sulfapyridine was more toxic than sulfathiazole. Six out of seven animals showed marked mechanical alteration in the genito-urinary tract and in addition primary renal damage. Widespread pyelonephritis with a rise in non-protein nitrogen was almost invariable. In addition to the glomerular damage there was extensive leucocytic infiltration about tubules filled with crystals of the drug. All animals showed a steady and significant reduction in neutrophiles in the blood and loss of weight.
E. S. MILLS

Studies on the Preservation of Human Blood. Kalmer, J. A. and Howard, M.: *Am. J. M. Sc.*, 1940, **200**: 311.

This study was undertaken to determine whether blood is better preserved by the addition of dextrose or of dextrin than when plain citrate or the Moscow Institute of Hæmatology mixture is added. Blood from two adult donors, mixed with the four different preservatives, was kept for 21 days at 4 degrees to 6 degrees C. Examinations of the four samples were made within 24 hours and at the end of 3, 5, 7, 10, 14 and 21 days' preservation. These included tests for dehæmoglobinization, fragility, and preservation of erythrocytes, preservation of leucocytes, preservation of platelets and prothrombin, and also the preservation of iso-agglutinins, complement and bactericidal activity.

They found that the two carbohydrate preservatives gave better protection of erythrocytes against dehæmoglobinization, fragility and disintegration, than the plain citrate or Moscow Institute of Hæmatology preservatives. Marked reduction in leucocytes and platelets occurred within three days with all four preservatives, but there was better preservation with the carbohydrate solutions. A slight decrease in prothrombin time (Howell) was observed with the plasmas of all preserved bloods within 24 hours, due to disintegration of platelets. During the following 3 to 7 days the blood deteriorated further in this respect, due to loss of prothrombin. Iso-agglutinins and bactericidal activity for *B. typhosus* was well preserved in all for at least 7 days.

Preserved blood should not be used in the treatment of infections, anæmias, or hæmorrhagic states unless dextrose or dextrin is added, although satisfactory for the treatment of surgical shock. E. S. MILLS

Hygiene and Public Health

Present Status of Knowledge Concerning Influenza. Horsfall, F. L.: *Am. J. Pub. Health*, 1940, **30**: 1302.

In this article Horsfall summarizes the work on influenza which has been done since 1933. In that year Smith, Andrews and Laidlaw recovered a virus pathogenic for ferrets from the throat washings of patients with influenza, and demonstrated that antibodies against the virus were produced during convalescence. Since

this discovery other workers have, in general, confirmed the findings, and a large number of strains of virus have been recovered from patients with the disease.

There is no reasonable doubt that this virus has been the cause of many influenza epidemics during the past seven years, but there is also little doubt that there have been some epidemics of apparent influenza which have not been caused by it. Unfortunately no characteristic signs and symptoms have been established which would serve to differentiate cases of influenza of known etiology from cases of unknown etiology. It is proposed to call the influenza due to the Smith, Andrews, Laidlaw virus Influenza A. In the event of other causative agents being discovered the disease could be called Influenza B, C, D, etc.

With respect to the influenza A virus some facts are of interest. The virus, in the first place, is filterable and ultramicroscopic. It may be identified by inoculation of throat washings into ferrets or by serological tests. These tests are either the complement fixation or the neutralization tests. They are easier to apply than the inoculation test, but inasmuch as time must elapse from the beginning of the disease until the development of antibodies it is not usually possible to obtain evidence of antibodies until ten days or two weeks have elapsed from the beginning of symptoms.

In the past seven years many strains of influenza virus have been recovered. It was at first thought that these strains were antigenically identical, but recent work has shown that this is not so. It is possible, however, that human antibody response may result in an immunity broad enough to protect against more than one strain of virus.

With regard to immunity there is good reason to believe that the immunity to influenza, unlike that developed after infection by many other viruses, is comparatively short lived. Francis and others have found that antibody titres declined about 50 per cent in from two and a half to five months after infection and determinations by the author of the antibody content of the sera of fifteen patients with proved influenza A show a fall of 80 to 90 per cent within a year after infection.

Attempts have been made to prepare vaccines for influenza A, but so far no convincing evidence has been obtained that these vaccines are effective, although there is some hope for the future development of a useful vaccine.

FRANK G. PEDLEY

Typhoid Vaccine Studies, Revaccination and Duration of Immunity. Longfellow, D. and Luippold, G. F.: *Am. J. Pub. Health,* 1940, **30**: 1311.

An important objection to typhoid vaccination as a means of preventing typhoid fever is the comparatively short protection which it is thought to give. The period of protection is uncertain, but for administrative purposes is assumed to be two years. No unequivocal test has been found which will tell easily the degree of immunity to typhoid fever possessed by an individual at any time, but the so-called mouse protection test does measure the circulating antibody content of the serum and is therefore thought to be a measure of the degree of immunity to natural infection.

The blood sera of 107 persons who gave no history of typhoid fever or inoculation were tested by the mouse protection test, and it was found that 83 per cent protected mice against less than 10 m.l.d. of organisms; 6 per cent protected mice against 100 m.l.d. The fairly high degree of immunity of the 6 per cent might be accounted for by unknown exposure or unrecognized disease. The sera of 20 of 21 children failed to protect mice against 1 m.l.d. On the other hand, study of the sera of 9 convalescent cases and 9 carriers showed that all protected mice against 100 m.l.d. or more of organisms. The authors believe that an individual may be regarded as immune to ordinary typhoid infection if his blood serum protects mice against 100 m.l.d. of virulent organisms.

On the basis of this assumption it was found that 2 weeks after initial vaccination (3 injections) all of 149 individuals demonstrated sufficient antibody; 12 to 18 months after initial vaccination 33 of 161 persons (21 per cent) had serum antibody below the 100 m.l.d. level, and 2½ to 3 years after initial vaccination 54 of 95 persons (57 per cent) had serum antibodies below that level.

Several methods of revaccination were studied and on the basis of the mouse protection and taking into consideration ease of administration, local reactions, etc., the authors recommend that the method of choice for revaccination should be 0.1 c.c. of vaccine administered intracutaneously. As second choice 0.5 c.c. of vaccine subcutaneously might be used. The interval between revaccination should be one year and certainly not more than two years. FRANK G. PEDLEY

Obituaries

Dr. James Franklin Adams, of Windsor, Ont., died on January 10, 1941. He was born in 1892 and a graduate of the University of Toronto (1916); L.R.C.P. (Lond.) and M.R.C.S. (Eng.), 1918.

Dr. Henri Desmarais, of Coderre, Sask., died on January 21, 1941, in his sixty-third year. Dr. Desmarais was a native of Three Rivers, Que., and was the son of the late Mr. Justice O. Desmarais, of the Superior Court and brother of Judge Jules Desmarais of the Court of Sessions. He was educated at St. Hyacinthe College and later at the Laval University (Montreal Division Medical School), receiving his doctor's degree in 1904. For several years he was on the staff of the Hotel-Dieu Hospital. He came west in 1910 and settled in the Coderre district, practising his profession until about two years ago when ill health forced him to retire.

Dr. Foster Fitch Eaton, prominent figure in the medical life of Truro, N.S., and the surrounding district, died suddenly on January 17, 1941. He was born in 1863. An outstanding physician, he was much loved by all in every walk of life and would if he had lived have observed his 51st anniversary in medical practice in May. As an active and valuable member of the Colchester and East Hants Medical Association, he had observed his 50th anniversary this year.

Deceased was a graduate in medicine from the University of New York (1889) and throughout his lifetime worked for the progress of the profession. For several years and at the time of his death he was Medical Health Officer for the town of Truro. Although in failing health, he had just discontinued active practice a week before he died.

Dr. Franklin Hanna, of Brantford, Ont., died on January 9, 1941. He was born in 1856 and graduated at McGill University (1879).

Dr. William Lane Holmes, of Victoria, B.C., died on December 26, 1940. He was born in 1857 and graduated from Bellevue Hospital Medical College, New York, in 1889.

Dr. Frank Charles Lavers died at his home in New Ross, N.S., on January 16, 1941. His death followed an illness of several weeks. He was seventy-five years of age. Dr. Lavers was born in Georgetown, P.E.I. In 1891 he graduated in medicine from Queen's University and came to New Ross. A few months hence he would have celebrated fifty years of a practice rich in good work.

Dr. John Thomas McCullough, of Nipawin, Sask., died on January 8, 1941. Dr. McCullough was born at St. Mary's, Ont., in 1887 and was a graduate of McGill University (1919). Thirty-three years ago he homesteaded at Tugaske, later teaching school for five years. During the Great War he served in the Flying Corps. Following the end of the War, he practised medicine at Kelliher, Sask., and for a number of years later at Craik and Ituna. In 1937 he came to Nipawin.

Dr. Kennedy Crawford McIlwraith, of Toronto, died on January 22, 1941, in his seventy-third year. He was a graduate of the University of Toronto (1894) and Emeritus Professor of Obstetrics there.

Dr. Alexander Munro, who practised medicine in Montreal for over half a century, died at his home, Westmount, in his 98th year on January 12, 1941.

Dr. Munro, son of Hector Munro and Jeannie Burnett, was perhaps the oldest graduate from the Medical School of McGill University, having obtained his degree in 1876.

Leaving school at an early age, young Munro went to work in the old Hart Drug Store that used to be on the south side of Notre Dame Street near St. Peter, but continued his studies until such time as he was able to save enough money to go to the university. After his graduation Dr. Munro went to London, England, and was an intern in the St. Thomas Hospital. Then he took post-graduate studies in Edinburgh and Paris.

On his return to Montreal Dr. Munro commenced to practise as a physician and surgeon on Beaver Hall Hill, which, in the early eighties was then the fashionable residential district of Montreal. Later he moved to Dorchester Street West, remaining there until 1910, when he established his home and office on Western Avenue. He retired from practice ten years ago. He enjoyed good health virtually all his life until two years ago, when his advanced age began to tell on him.

Dr. Thomas Fulton Robertson, of Brockville, Ont., died on January 29, 1941. He had practised in Brockville for nearly fifty years. He was a native of Spencerville, Ont., born in 1869, and a graduate of McGill University (1891). Dr. Robertson was Chairman of the Public Utilities Commission in Brockville several times and was senior coroner for Leeds County.

Dr. Rosaire Rolland, chief medical officer of the port of Montreal, died on January 24, 1941, in his 49th year.

A native of Montreal, Dr. Rolland completed his early studies at St. Laurent College and graduated in medicine from University of Montreal in 1923. He then was attached to the Hotel-Dieu Hospital where he became chief of interns. Dr. Rolland served with the Department of Immigration and travelled extensively in Europe.

In 1937 he was appointed assistant to Dr. G. E. Beauchamp who was then chief medical officer of the port of Montreal, and later succeeded him in that position.

Dr. John Winfield Rush, of Toronto, died on January 17, 1941. He was born in 1893 and a graduate of the University of Toronto (1920).

Dr. Thomas Duncan Rutherford, of Burford, Ont., died on December 10, 1940. He was born in 1880 and a graduate of the University of Toronto (1905).

Dr. Allen Avery Shepard, of Sault Ste. Marie, Ont., died on December 2, 1940. He was born in 1873 and a graduate of the University of Toronto (1898).

Dr. Charles Tupper Weeks died at Tidnish, N.S., on January 10, 1941. He was born in 1860. A graduate of the University of Baltimore (1885), Dr. Weeks spent the great part of his life in practice at Cambridge, Mass., returning to his native village on his retirement six years ago.

Dr. Thomas Wickett, of Hamilton, Ont., died on January 12, 1941. He was born in 1863 and a graduate of the University of Toronto (1894).

News Items

Alberta

The regular meeting of the Council of the College of Physicians and Surgeons of Alberta was held in Edmonton, January 22, 1941, when Dr. R. B. Francis was elected President for 1941 and Dr. W. G. Anderson, Vice-president for the same period. The Council also elected these two physicians as representatives on the Medical Council of Canada for a four year period, commencing with the present year.

The Cancer Committee presented its report to the Council for consideration. It was afterwards presented to the Government and was favourably received. Among the recommendations regarding the work being undertaken by the Government in dealing with the cancer problem the Committee suggested that it was unwise for members of the staff of the Diagnostic Clinic already established to personally treat the patients. This, of course, would depend on the conditions existing in any local diagnostic centre. It was thought that if biopsies were necessary they should, if possible, be done by the surgeon who is going to carry out the subsequent surgical treatment. Radiological diagnosis and treatment should be carried out by utilizing all available competent radiologists. Full reports of the examination should be sent back to the referring physician. The Committee recommended that the plan should provide for the using of all capable and competent physicians in cancer work.

The Council discussed with representatives of the Workmen's Compensation Board the new schedule of fees to become operative, commencing February 1, 1941. What is noted is that the new list covers many cases not previously specified in former lists. While the schedule of fees will cover the ordinary work in

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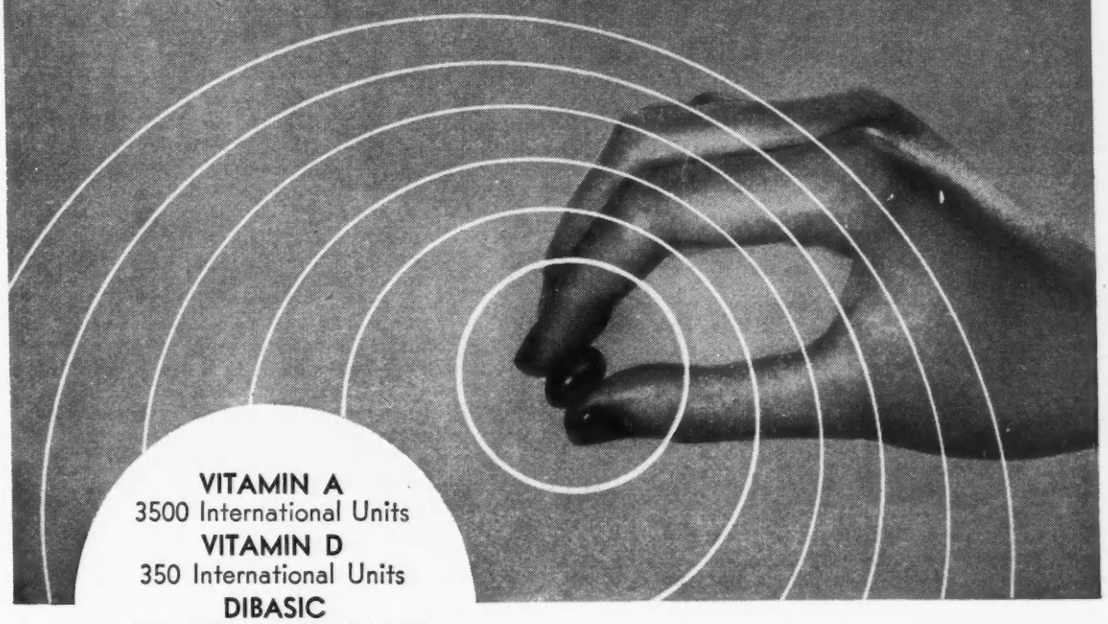

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the general cases, it is specifically provided that in difficult cases the Board will pay greater fees based on the seriousness of the case and the actual amount of care necessary. In minor injuries the maximum fee is set down as $11.00 for the first 8 days, namely, $3.00 for first treatment and report, and $8.00 for the next 7 days with a $5.00 limit for each week for the next 3 weeks. Office dressings to remain as formerly, but hospital visits are reduced to $1.00 per visit.

The Council made the following grants: University Medical Library, $200.00; Calgary Medical Library, $100.00; History of Medicine, $75.00; University Medical Scholarships as formerly, 5 at $50.00 each.

The following new registrants were reported: Drs. William P. Goldman, Edson; Thomas R. Clarke, Edmonton; Bruce C. Hardy, Edmonton; Walter S. Anderson, Edmonton; Leo L. Giroux, Edmonton; N. H. Olesker, Fairview; Ralph G. Martin, Calgary; Jacob B. Mandel, Saskatoon.

The financial statement of the College of Physicians and Surgeons of Alberta showed total assets of $49,000.00; $1,800.00 is cash on hand, and $35,000.00 Government bonds. The Council holds a mortgage for $3,500.00; the balance is for fees due by members, many of which were just of one year's standing.

The Council discussed the question which was raised in another province of transferring all power of licensure to one body, but lacking details from the mover, as to the benefits to accrue to anybody except the new registrants, the matter was held over for further consideration.

Dr. C. E. Anderson, who has been practising at Brooks, has joined the R.C.A.M.C. and is stationed at Edmonton. Dr. S. F. Carr, of Rimbey, has taken over the practice.

The session of the Legislature is called for February 20, 1941, and the following members of the profession will attend as members: Hon. Dr. W. W. Cross, Minister of Health; Drs. J. L. McPherson, Social Credit member of Ryley; L. J. O'Brien, Independent, Grande Prairie; P. M. Campbell, Independent, Lethbridge.

Strong protests are heard from physicians who are working in clinics or under municipal contracts because of the ruling of the Department that they are not allowed a deduction for the necessary expenses in connection with their practice as are permitted by men in general practice, where the fees are directly collected from the patients. It is felt that someone, in advising the Department at Ottawa, had in mind only the doctors working directly under Governments on salary where the Government pays all expenses. A strong protest is being made to Ottawa.

Dr. E. P. Scarlett, F.R.C.P.(C.), of Calgary, was the guest speaker at the Toronto Academy of Medicine, held on January 7, 1941, to commemorate the four hundredth anniversary of the death of Paracelsus.

The diagnostic cancer clinic, under the auspices of the Provincial Government, was opened in Edmonton on January 14, 1941. This is the first of its kind in Alberta. Dr. G. H. Malcolmson, new director of Cancer Services for the Province, is in charge, while on the assisting staff are Dr. John MacGregor, pathologist, Dr. W. C. Whiteside, surgeon; Dr. E. F. Donald, physician. Dr. Malcolmson is also acting as radiologist until increased demands make a change necessary. The clinic will be held once a week.

G. E. LEARMONTH

British Columbia

Vancouver was visited recently by Dr. Charles Walter Clarke, Executive Director, American Social Hygiene Association. He addressed a luncheon meeting of the British Columbia Medical Association and later a meeting of the Greater Vancouver Health League. Both meetings were well attended, especially the latter which directed a large attendance from the general public. This latter meeting was in connection with the Social Hygiene week of the League, and Doctor Clarke's visit was both timely and valuable.

At the meeting at which he addressed the British Columbia Medical Association he emphasized the seriousness of the venereal disease hazard in war time and the urgent necessity for the help of physicians in reducing to a minimum the possibility of infection by the civilian population. He referred to commercial prostitution as an "alien fifth column" undermining the efficiency of the war effort by its effect not only on soldiers but on potential recruits and members of key industries.

In connection with this campaign against venereal disease, it is of interest to note that the City of Vancouver is at the present moment, through its police commission, engaged in a definite attack on the question of commercial prostitution. A recent decision by Magistrate Wood, based on a provision in the Criminal Code hitherto, one must suppose, overlooked, that owners of houses used for this purpose may under certain conditions be regarded as keepers of bawdy houses, has given the police a very valuable and powerful weapon, and a conviction on this basis has resulted in many owners in the city giving notice to tenants, who are obviously carrying on the trade, so that they may themselves get out from under. In many cases these owners have been repeatedly warned by the police, and knew very well the purposes for which their houses were being used, but had considered themselves immune and took no steps to assist in enforcement of law.

The members of the medical profession in British Columbia have received a copy of the articles by Mr. Hugh H. Wolfenden in book form with a foreword by Dr. Wallace Wilson, Chairman of the Committee on Medical Economics of the Canadian Medical Association. This book constitutes a valuable collection of articles which we have all read with great interest and are glad to have available for further study.

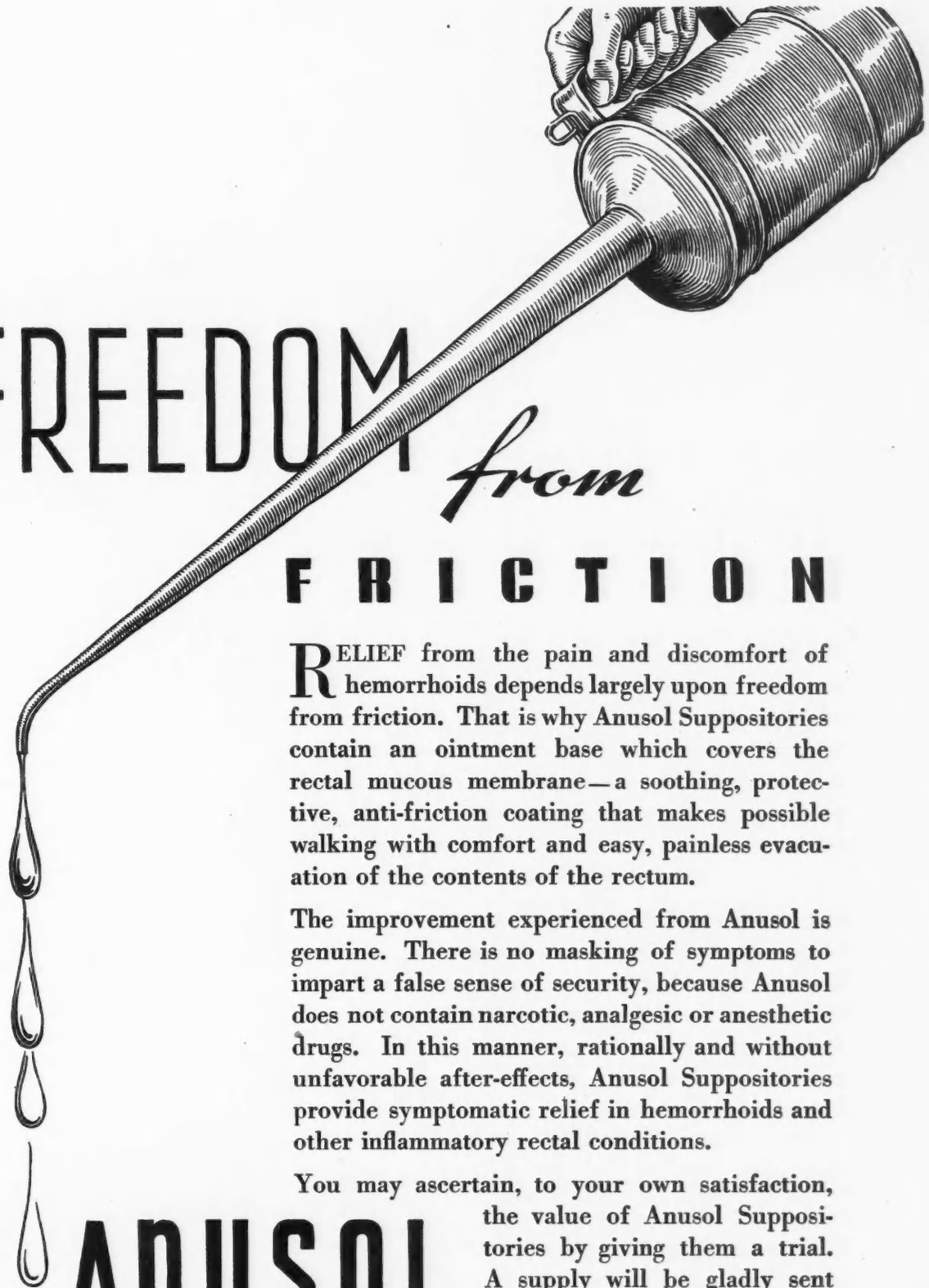
Recent accessions from the British Columbia profession to the military forces of the country are the following: Dr. F. E. Coy of Invermere, Dr. R. J. Wride of Princeton, Dr. B. L. Dunham of Nelson and Dr. W. Roy Walker of Penticton.

In connection with the British Columbia Cancer Institute a very useful movement was made in the Institute of open meetings to which the profession is invited, where members of the staff conduct a symposium on different aspects of the cancer situation. These are being well attended and are of great interest to the members of the medical profession.

J. H. MACDERMOT

Manitoba

The annual meeting of the Sanatorium Board of Manitoba was held on February 4th. Mr. John McEachern, a past-president of the Canadian Tuberculosis Association was unanimously re-elected president. In his report Dr. E. L. Ross, Medical Superintendent, stated that although the number of far advanced cases admitted to Ninette Sanatorium had been cut in two in twenty years, there were still 45 per cent in this class. The use of the bronchoscope in diagnosis and treatment had been doubled in the past year with very satisfactory results. The treatment of tuberculous tracheo-bronchitis by the application of a 35 per cent solution of silver nitrate had been found very useful. There was no operative mortality following surgical operations, although a considerable number of operations, including 80 stages of thoracoplasty, had been done at the Sanatorium. One hundred and fifteen adults were benefited by the school. Christmas seals had shown an increase in receipts of 18 per cent. Dr. D. L. Scott, Assistant Medical Superintendent, reported that 216 new cases of tuberculosis were discovered at the Central Tuberculosis Clinic in Winnipeg. Dr. M. H. Campbell, Resident Physician



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of Dynevor Indian Hospital, stated that children under the age of 15 constituted 42 per cent of admissions.

On January 30th Prof. I. Maclaren Thompson gave an address on "Edinburgh contributions to female pelvic anatomy", before the Sections of Historical Medicine and of Obstetrics and Gynæcology of the Winnipeg Medical Society. Prof. Thompson referred to the work of such men as John Goodsir, Sir William Turner, Halliday Croom, David Hart, A. H. Barbour, and Clarence Webster, and illustrated his remarks both with lantern slides and with books and monographs in this field by these anatomists and gynæcologists.

The late Edward L. Drewry left a bequest of $1,000 to the Sanatorium Board of Manitoba of which he had been a member for many years.

The Board of Trustees of the Winnipeg General Hospital has appointed Dr. Harry Coppinger as Acting Superintendent and Mr. F. W. L. Judge, Business Manager.

The Manitoba Hospital Service Association has had a successful year's operation. The number of participants is now 37,000.

Dr. M. S. Lougheed, Medical Health Officer of Winnipeg, is making a test tuberculin survey following a grant of $500.00 from the City Council.

The second annual Dr. David A. Stewart Memorial Lecture was delivered in the Manitoba Medical College on February 12th by Dr. Ross Mitchell. Dr. J. D. Adamson presided, and President Sidney Smith, members of the Sanatorium Board, the Medical Faculty, and third and fourth year medical students were present.

ROSS MITCHELL

New Brunswick

The Health Bureau Meeting was held in Fredericton on January 29th under the chairmanship of the Chief Medical Officer, Dr. C. W. McMillan. The Minister of Health, Hon. J. A. Doucette opened the meeting with remarks on the importance, at the present moment, of venereal disease in wartime and tuberculosis. After much discussion a committee was oppointed composed of Dr. C. W. McMillan, Dr. J. M. Cameron, Dr. R. A. H. McKeen to explore the problem of venereal disease as thoroughly as possible regarding legislation and publicity with the view to arriving at some more or less uniform legislative scheme of action.

Concerning diphtheria it was the opinion of the meeting that more efforts should be made of continuous publicity to obtain a more universal response to the immunization of infants and preschool children. The bureau recorded its regret at the enforced retirement of Dr. Wm. Warwick due to ill health.

Dr. V. D. Davidson, Surgical Specialist of the Department of Pensions and National Health for New Brunswick, has been confined to hospital for some time by illness and has now returned to duty following a short convalescence in the Laurentians.

Dr. W. J. Baxter of Fairville, N.B., is convalescing satisfactorily following an attack of pneumonia.

Dr. R. J. Dolan, South Nelson, N.B., has joined the Royal Army Medical Corps, Active Service, and is at present stationed at Saint John.

Dr. R. F. Chaisson, of Saint John, has been gazetted a Lieutenant in the R.C.A.M.C. (R.F.) and attached to No. 14 Field Ambulance.

Dr. DuVernet Jack, of Glenwood, N.B., is confined to his home by illness.

Capt. F. C. Jennings, R.C.A.M.C., No. 7 Detachment, Saint John has been granted his majority and is now officer in charge of hygiene for the district.

The following officers have been appointed to command hospitals in Military District No. 7: Capt. H. E. Baird to command Neill Hospital, Fredericton; Major Jos. Tanzman to command Howe Lake Hospital, Saint John; Major R. M. Pendrigh to command St. James Street Military Hospital, Saint John.

The regular monthly meeting of the Saint John Medical Society was held in the Admiral Beatty Hotel on January 28, 1941, with Dr. Douglas Gibbon chairman. The special speaker was Dr. W. A. Clark, Provincial D partment of Health, whose subject was "Carriers and subclinical infections".

Dr. W. O. McDonald was the special speaker at the meeting of the Life Underwriters' Association at Saint John on January 30, 1941. His subject was "Blood transfusion".

Dr. Gilbert Turner, of Fredericton, is now Squadron Leader Turner of the Royal Airforce Medical Corps stationed in Ontario.

A. STANLEY KIRKLAND

Nova Scotia

From the Harvard Medical School a group of epidemiologists has come to Halifax to study the communicable disease situation at the eastern Canadian port. Heading the mission is Dr. John H. Mueller, associate professor of bacteriology and immunology; associated are Dr. Leroy D. Fothergill, also of bacteriology and immunology, Dr. Emanuel B. Schoenbach, bacteriology, Dr. John Dingle, medicine, Dr. Stafford M. Wheeler, preventive medicine and epidemiology, Dr. Lewis Thomas, medicine. Completing the party is a group of technicians. Said Dr. Mueller: "The information we gather will be of great assistance in combating similar outbreaks in United States military camps. That is one of the main reasons we came." Bringing back memories of the abundant Massachusetts aid after the Halifax explosion, 1917, the visitors got a warm welcome. They are working under the Department of Health, and in conjunction with Dr. Allan Morton, City Health Officer.

Remodelling and re-opening two pavilions at the Kentville sanatorium increase its bed capacity to 370.

To June, 1940, the Dalhousie Public Health Clinic deficit was $178,000. "That," said President Carleton Stanley, "is a contribution Dalhousie has made to the City of Halifax." Really touched for the first time in many such appeals, the City increased the Clinic's annual grant from $5,000 to $10,000.

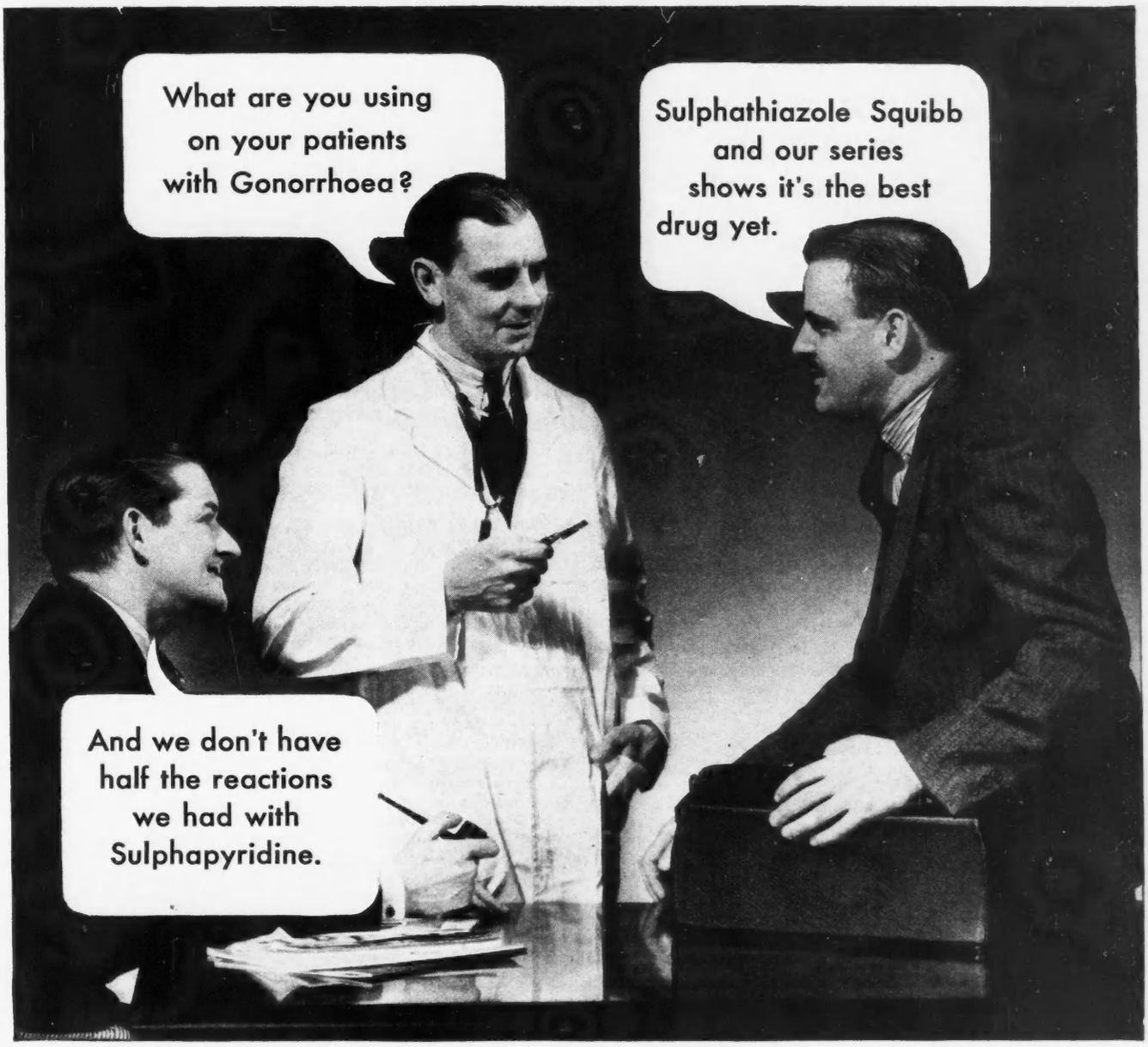
Donning of khaki by Dr. C. H. Baker, Middle Musquodoboit, leaves another thirty mile stretch of Halifax County without medical attendant.

Hospital bed capacity in Halifax has been increased to a slight extent by the opening of a thirty-room annex to the City Infectious Disease Hospital.

Prominent in the Bear River Board of Trade for 1941 are Dr. L. J. Lovett as president, and Dr. A. B. Campbell, council member.

A fifty-bed Red Cross emergency hospital and clearing station has been set up at Sydney Mines.

Dr. Max D. Brennan has returned to Dartmouth from Cook County Hospital where he has been doing postgraduate work.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Dr. Clarence Gosse (Dal. '39), has been awarded a fellowship in surgery at the Crile Clinic.

The Red Cross Blood Donor Service, getting under way at Halifax, already has three hundred volunteers. While offering their blood for emergency service, these donors may also be available for routine hospital work at the regular rates. ARTHUR L. MURPHY

Ontario

Colonel D. A. Warren, formerly President of the Hamilton Academy of Medicine, has been appointed Officer in Charge of Chorley Park Convalescent Hospital recently established in M.D. No. 2. It is a hospital of 200 beds and has been commanded temporarily by Lieut.-Colonel A. B. James. It is the former residence of Ontario's Lieutenant-Governor. The refectory of the Hospital has been given up to the preparation of parcels for prisoners of war. This work is being done for the Red Cross by a group of graduate nurses who served in the R.C.A.M.C. during the last war.

Dr. W. J. Chapman, St. Catharines, has been re-elected President of the Ontario Municipal Electric Association.

Dr. R. J. Galloway, one time Varsity football captain, has been appointed doctor to the Maple Leafs hockey team.

The many friends of A. R. Hagerman, who has been, for some time, a District Medical Officer, M.D. No. 2, are very pleased to note that he has been granted the rank of Colonel in the R.C.A.M.C.

The 14th annual banquet of the Osler Society of London was held on January 24th, with Dr. W. G. Penfield, of Montreal, as the guest speaker. Over 150 were present. Dr. Penfield recalled to the students the many instances of his residence in Oxford as a Rhodes Scholar and of his convalescence in Osler's home as a war casualty.

Dr. G. C. Brink, Director of the Division of Tuberculosis Prevention of the Department of Health, Ontario, has issued his annual report for the year 1939. The tuberculosis death rate in Ontario reached its lowest point in 1938, *viz.*, 33.1 per 100,000 population, while 54.7 was the rate for Canada as a whole during the same year. There has been a steady decline in the tuberculosis death rate since 1930.

The Department is encouraging tuberculosis surveys of apparently healthy individuals in the age-group 20 to 40 years. In order to detect unrecognized cases, a number of the larger general hospitals in Ontario have been asked to take routine chest x-ray films of all patients admitted to the public ward. Five hundred or more will be taken in some of the hospitals in an attempt to estimate the number of unrecognized cases.

There has been an increase in the number of sanatorium beds.

The work of the travelling clinics is outlined, and, from a study of the tables, it is quite evident that a large number of cases of tuberculosis have been discovered during examination as contacts, who if they had waited until the development of symptoms would have been in advanced stages of the disease.

Each year a number of Indians living on reserves in Ontario are being examined. The death rate among Indians in Ontario does not seem to be as high as in the Western Provinces.

The Department continues to insist upon the tuberculin test and x-ray examination of all nurses in public and general hospitals, hospitals for incurables, and in sanatoriums.

It is noted that artificial pneumothorax treatment had been, or was being, applied to about 58 per cent of the patients who are in sanatoriums at the time of the survey. J. H. ELLIOTT

Quebec

Without regard to party affiliations, members of the Public Bills Committee voted on February 19th against a bill aiming to incorporate the Quebec Chiropractic Association. The vote was 10 to 7, which means that for the third time, the measure was refused by the Legislature.

Le Conseil de la Faculté de médecine de l'Université de Montréal vient d'approuver l'institution d'une épreuve d'agrégation aux chaires suivantes: Phtisiologie, Anatomie, Anatomie pathologique, Médecine légale et Dermato-syphiligraphie.

Le Dr Albéric Marin vient d'être élu président de l'*Union Médicale du Canada*. Il succède au Dr R. E. Valin. Le seul autre changement parmi les officiers est la nomination du Dr C. A. Gauthier (de Québec) au poste de deuxième vice-président.

A l'Hôtel-Dieu de Montréal, le Dr Oscar Mercier devient président du Bureau exécutif, et le Dr Albert Jutras, président du Bureau médical.

L'Action Universitaire, revue mensuelle des diplômés de l'Université de Montréal, consacrait son numéro de janvier à la Faculté de Médecine. Trois articles importants mettent bien les choses au point: La Faculté de Médecine par le doyen Albert LeSage; les laboratoires de la Faculté par le Dr Georges Baril, et l'Institut de Microbiologie par le Dr. Armand Frappier.
JEAN SAUCIER

Saskatchewan

The January meeting of the Regina and District Medical Society was addressed by Major J. C. Paterson of the Eighth Base Hospital, formerly pathologist to Ottawa Civic Hospital. His subject was "Coronary thrombosis".

Members of the Regina and District Medical Society passed a resolution to operate gratuitously on cases of hernia in indigents who were desirous of enlisting and in whom the hernia was the only thing keeping them from being accepted. This offer was accepted by the military authorities.

Ten Outpost Hospitals are operated by the Red Cross in Saskatchewan. In 1940 they cared for 452 maternity cases with no maternal deaths. There were 9 still births and 7 neonatal deaths. In February, 1940, a new Outpost Hospital was opened at Hudson Bay Junction. LILLIAN A. CHASE

General

Reciprocity with Italy. — The General Medical Council of Great Britain in 1901 established reciprocity with Italy, whereby graduates in medicine of Italian universities could register on the Foreign List without further examination. On October 11, 1940, this regulation was revoked, without prejudice, however, to the rights of any persons whose names already appear in the Medical Register.

Britain to License Canadian and United States Physicians.—Canadian and United States physicians are being licensed by Great Britain for the duration of the war. The government (British) has made an order under the Emergency Powers Act, passed for the purposes of the war, enabling the General Medical Council to register for the period of the emergency Canadian and United States physicians. These will thus be able to join the Emergency Medical Service with the same privileges as British physicians.

A New Journal on Medical Care.—The widespread need for more adequate medical service voiced by President Roosevelt in his recent message to Congress will now be dealt with in a special periodical *Medical Care*, a quarterly, the first issue of which appeared on

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In treatment and prevention of localized staphylococcal infections such as styes, boils, carbuncles, pustular acne and recurrent staphylococcal abscesses, **Staphylococcus Toxoid** has proved to be distinctly effective. This product is a non-toxic antigen, prepared by treating highly potent staphylococcus toxins with formaldehyde, and cannot induce sensitization to any antitoxin or serum.

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January 21, 1941. The new journal is a non-profit enterprise under the auspices of the Committee on Research in Medical Economics, Inc., 1790 Broadway, New York, with Michael M. Davis, Chairman of this Committee, as its Editor. Williams & Wilkins Company, of Baltimore, are the publishing agents. Its stated purposes are "to disseminate information concerning the economic and social aspects of medicine, to promote a scientific approach to the subject, and to stimulate practical action by the professions and the public in their common interest. The views and interests of the professions that furnish medical care and of the people who receive it are equally to be considered.

Among the articles to the first number are: "British medical arrangements for the care of air-raid victims", by Dr. George F. McCleary, formerly of the British Ministry of Health; "Preparedness through fitness", by Dr. Nathan B. Van Etten, President of the American Medical Association; "A health program for California farmers", by Von T. Ellsworth, Director of the California Farm Bureau Federation; "The costs of physicians' services under a voluntary health insurance plan", by Helen Hershfield Avnet, of the Group Health Co-operative, New York. One of the editorials urges adequate medical care for industrial workers in defense industries, as a means of promoting the productive efficiency which the nation needs. The federal government's organization up to date for dealing with health problems arising out of the national defense program is described in the department of Current Events, which also contains a review of what twenty-four state medical societies did during 1940 concerning voluntary health insurance plans.

Future issues will include a Forum, open to signed expression of opinion by laymen and physicians; current news of legislation and private action in the field; and reviews of books, articles, and pamphlets concerning the economic and social aspects of medicine. The new journal has a group of about 45 editorial advisors, including members of the medical and allied professions, social scientists, public administrators, and men and women representing the general public interest; and an efficient editorial board.

Book Reviews

Fractures and Dislocations. E. O. Geckeler. 2nd ed., 314 pp., illust. $4.00. University of Toronto Press, Toronto, 1940.

This small book is a revised edition and is prepared specially for general practitioners dealing with fractures and dislocations. The script is lucidly written and the methods advocated simple and conservative. Little attention is given to open operative procedure, and the author confines himself to one proved method. The text is well illustrated and arranged.

The book as a whole will be found useful to those dealing with occasional fractures, but it is not sufficiently detailed for workers dealing with the whole field of traumatic bone surgery.

Clinical Diabetes Mellitus and Hyperinsulinism. R. M. Wilder. 459 pp., illust. $7.00. McAinsh, Toronto, 1940.

This monograph follows a very extensive experience in treating patients with diabetes mellitus, the author having been in charge of this branch of medicine at the Mayo Clinic for many years. It is essentially clinical in its appeal, and methods of diagnosis and treatment are stressed throughout. Only generally accepted methods are advocated. While orthodox, it is at the same time individualistic. It may be recommended to any practitioner wishing a clear presentation of the treatment of this common disease, diabetes, and its numerous complications.

The chapter on diagnosis with the interpretation of dextrose tolerance tests and non-diabetic meliturias is one of the best in the book. Acidosis and coma are adequately stressed. In the section headed Substitution Therapy the author outlines a practical scheme for the regulation of the dosage of insulin, depending on the amount of urinary sugar as shown by Benedict's qualitative tests. Many will take issue with him on the advisability of administering protamine insulin zinc and unmodified insulin in the same syringe, as their acidity is different. There are chapters on diabetes in relation to surgical operations, complicating disorders of the eye, nervous system, digestive organs and skin which are interesting, informative and authoritative. The chapter on arteriosclerosis and diseases of the heart in diabetes is especially noteworthy. Hyperinsulinism is thoroughly discussed, probably out of proportion to its frequency and importance.

Diagnosis and Treatment of Menstrual Disorders and Sterility. C. Mazer and S. L. Israel. 485 pp., illust. $6.50. P. B. Hoeber, New York, 1941.

In a world where we are beset by the miraculous claims of hormone therapy this book has an unquestioned place. It may plough up no new fields, but it does pick its way through the subject in a very sane and restrained fashion. In short, it makes no outrageous claims for any particular forms of treatment or theory.

While more useful to those practising gynæcology, it is a book that any practitioner who is anxious to learn something about the subject matter it covers should certainly have on his shelves. Further, for those wishing to pursue the study farther it contains at the end of each chapter a very carefully chosen bibliography.

In a field like this where theory and therapy are being rapidly and often radically modified, there is a tendency for the textbook to lag and rapidly fall out of date. But in so far as our present knowledge goes this book is eminently up to the minute. In particular it is the sort of book that any doctor using the ovarian and pituitary hormones would find a steadying influence—and we can do with steadying influences where this type of therapy is concerned.

Clinical Practice in Infectious Diseases. E. H. R. Harries and M. Mitman. 468 pp., illust. $5.25. E. & S. Livingstone, Edinburgh, 1940.

This is a new book on the subject, written by two men who have had long experience in the English "Fever Hospitals" as well as in lecturing to medical students on infectious diseases. The material is largely from the authors' personal experiences and probably follows the lines of their lecture courses, but for the most part the usually accepted teachings are adopted. Various authors are quoted throughout the book, but a listing of the references unfortunately has been omitted.

The general arrangement of the book is excellent, having regard to the order in which the subjects are discussed and the presentation of material. The first part of the book deals with the theories of infection and immunity and general considerations in diagnosis, epidemiology, and management. The remainder of the book is devoted to the specific infectious diseases usually seen in temperate climates. The chapter on Infection and Resistance is an example of a difficult subject which has been handled in such a simple manner that the principles could be understood by a layman. However, many readers may wish for a more detailed and scientific discussion.

Each chapter is concluded with a short summary of the contents—almost too brief to be of great value. The illustrations are of a simple diagrammatic character, some in colour, and, as the authors suggest, are probably of more value than the usual vivid but misleading colour illustrations. Treatment has been rather briefly passed over and is somewhat dogmatic. This fashion of a previous generation seems to die slowly. The index is largely a listing of the paragraph headings which might be enlarged upon to advantage. On the whole it is a very readable and up-to-date contribution to the subject, and should appeal particularly to students and practitioners who wish to reacquaint themselves with the theory as well as the clinical aspects of these conditions.

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By Major T. G. Heaton, M.B.
Officer in Charge, Toronto Military Hospital; Late Chest Clinician, Toronto Western Hospital; Late of Mountain Sanatorium, Hamilton.

Foreign Bodies Left in the Abdomen. H. S. Crossen and F. Crossen. 762 pp., illust. $11.50. McAinsh, Toronto, 1940.

This is a new subject in one sense. Every surgeon knows the caution that has to be observed to prevent the leaving of foreign objects in the abdomen at operation, sponges, forceps, etc.; and, in spite of all caution, how often such accidents occur. But so far the subject has not been brought into the compass of a book. Next in importance to the technical aspect is the medico-legal standpoint of this subject. It is therefore of great value that the last five chapters of the book are devoted to the legal problems associated with the matter.

Surgeons will find the book of unusual interest, both in its scope, for it covers a very wide field, as shown by the cases referred to and the extensive bibliography, and in the medico-legal discussion.

Diseases of the Nervous System. F. M. R. Walshe. 288 pp., $3.75. Macmillan, Toronto, 1940.

This is a splendid book. In his preface the author states "I have tried to deal only with what is possible in general practice in the matter of diagnostic methods and of treatment, to strip the subject of unnecessary complexities, and to confine myself to what I have seen and believe to be true".

The book begins with an introductory chapter, and a long section on "Anatomical or localizing factors in diagnosis" which is in itself a masterpiece of teaching.

The main body of the book gives an account of the commoner organic diseases of the nervous system, which would be hard to equal. If one were to single out any part, to praise for its vivid descriptive writing, it would be his chapter on "Paralysis Agitans". The psychoneuroses are dealt with in a short chapter, stressing mainly the differential diagnosis from organic disease. A simple scheme of examination of the nervous system is given in the final chapter.

It seems fair to paint out certain limitations of this book as they appear to the reviewer. One would question his neglect of special methods of neurological diagnosis —even in an elementary text. Keen clinical observation undoubtedly remains the most important factor in diagnosis, but it is no exaggeration to say that newer x-ray methods of diagnosis alone, have added tremendously to the accuracy of neurological diagnosis over the past 15 years. Other than the examination of the spinal fluid, very little mention is made of laboratory methods of diagnosis. One would like to find more space given to the consideration of the commoner neurological symptoms such as headache, dizziness, paræsthesias, loss of consciousness, which are the everyday problems of the general practitioner. One would also like to see the treatment of neurosyphilis given in greater detail, with a clear outline of what is meant by "adequate" treatment of syphilis. Also, one would like to find in a book of this sort more general recognition of the psychological factors which are ever present in even the most "organic" of diseases. We deal in actual life not with diseases, but with persons suffering from disease, and it is time that our textbooks were written with this in mind. The book would undoubtedly be more useful if it contained more diagrams and drawings, and at least a few good general references.

With such limitations, this book can be heartily recommended to every medical student and doctor, and to all who practise and teach neurology.

Heart Failure. A. M. Fishberg. 2nd ed., 829 pp., illust. $9.75. Lea & Febiger, Phila., 1940.

The first part of the book is devoted to the individual manifestations of circulatory failure. In this portion are considered cardiac output, velocity of blood flow, the circulating blood volume, arterial pressure, pulse and alteration of pulse, venous pressure, and exertional dyspnœa, etc. Each individual manifestation of circulatory failure is reviewed from its experimental viewpoint, and following this its clinical application is discussed. The second section is concerned with the clinical picture engendered by circulatory failure, primarily from the point of view of the cardinal circulatory syndromes involved. The final section is apportioned to the treatment of patients with circulatory failure.

Since the first edition the author has included recent advances in clinical and experimental investigations. Many of these are concerned with quantitative measurements of some of the fundamental circulatory variations in health and disease. The practitioner or specialist is thus able to approach his patient with a better understanding of the dynamics of the diseased circulation, and better qualified to give effective treatment.

As in his other works, the author realizes the limitations of the general practitioner so far as complicated studies are concerned, and makes every effort to interpret the advances for the practising physician in a manner which will aid him in his daily duties. The book is well indexed, and the tremendous reference list makes it an ideal volume for the specialist and student.

Modern Dermatology and Syphilology. S. W. Becker and M. E. Obermayer. 896 pp., illust. $15.00. Lippincott, Montreal, 1940.

This is an excellent book and will prove most useful to the general practitioner and the dermatologist. Its simple language and choice of words make reading a pleasure; for example, the description of psoriasis as "a usually harmless but at times cosmetically disfiguring eruption" is a most apt expression.

Each chapter opens with a section entitled Orientation. The object of this feature is to give a practical description or presentation of the subject to be discussed in detail.

An earlier chapter describes diseases according to regional distribution, for example, those eruptions common to the axilla, the face or the trunk. This plan is not new, but, unlike so many texts, every known disease has not been included and it is of more value for this reason, especially to the general practitioner.

The chapter on etiology discusses climate and season. Many dermatological texts do not stress these factors. They are important in connection with diseases of the skin and especially in Canada where we are exposed to the drying effect of artificial heat at least seven months in the year.

The chapter dealing with drug eruptions and occupational dermatoses is specially interesting.

The illustrations, both coloured and black-and-white, are very good. The bibliography presents the important publications of the past five to ten years. The book is an excellent addition to modern dermatology.

Newer Nutrition in Pædiatric Practice. I. N. Kugelmass. 1155 pp., illust. $12.00. Lippincott, Montreal, 1940.

This is an extensive work on nutrition in health and disease which has plenty of practical information, although accuracy of detail is not always maintained. The author has applied the recent knowledge in nutrition to the problems of infant and childhood disease as well as those of growth and prevention of disease. There are three main sections. The first deals with the physical and chemical basis of growth and nutrition. The many factors concerned in these functions are discussed, particularly the physiology of absorption and metabolism. The second section deals with the maintenance of health by proper eating and details of food values in nourishment and digestibility are given. Section three comprises two-thirds of the book, and is of greatest interest to the practising physician in that it deals with the digestive and deficiency diseases, and provides helpful diet lists for their correction. The dietary factor in metabolic diseases is discussed. There is a chapter on allergy and many diets are presented in detail. The book contains much information that is a composite picture of dietary planning in a children's hospital, and such information is often difficult for the individual physician to come by. The author has provided a useful text for reference in all the dietary and feeding problems in children.